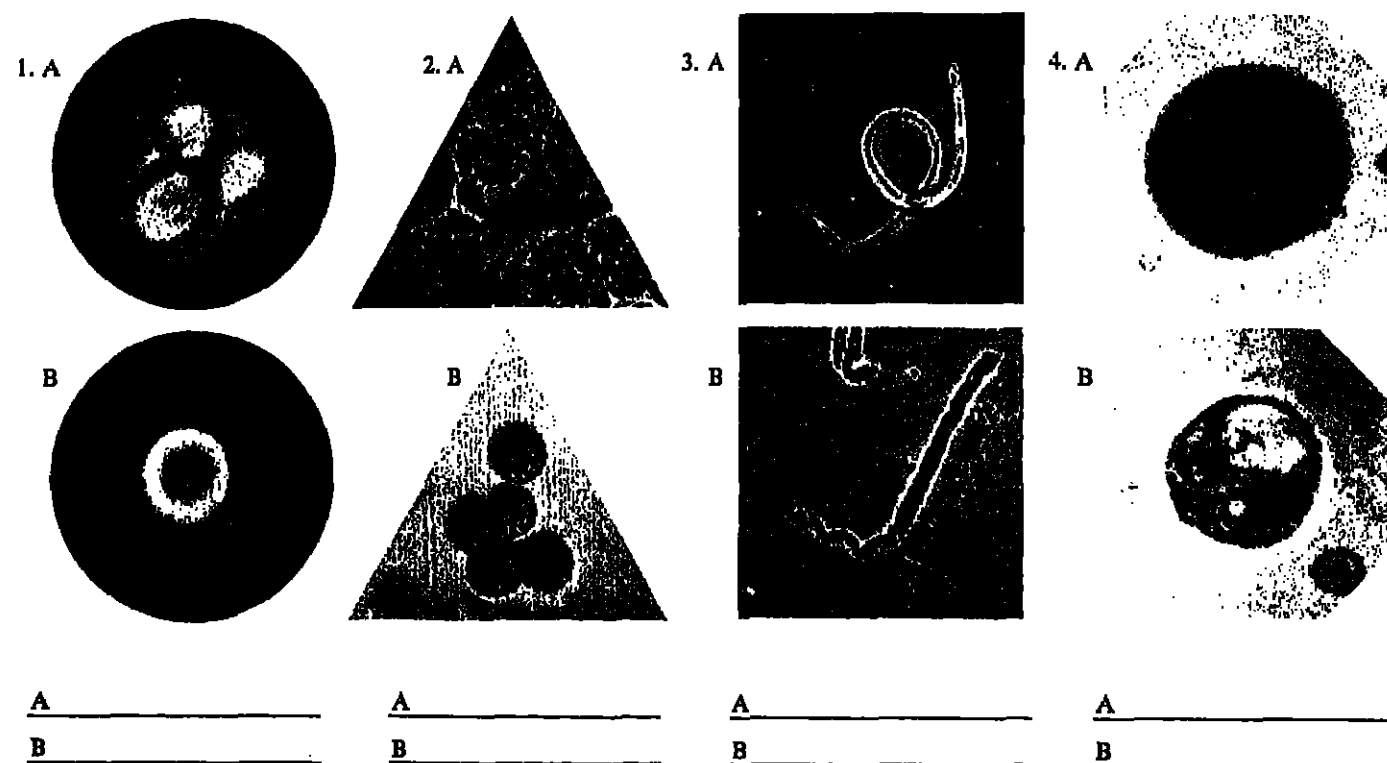


Puzzling Pairs

Can you identify these look-alike findings in urinary sediment? Spaces are provided below for your answers. One of a series of quizzes based on Roche's handbook, "Urine Under the Microscope."



For correct answers and identifying clues, see bottom of page.

No Puzzle Here



E. coli showing typical gram-negative rods. The coliforms—particularly *Escherichia coli*—are the primary pathogens in approximately 90 per cent of initial urinary tract infections.*

*Beeson, P. B.: "Enteric Bacterial Infections," in Beeson, P. B., and McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Philadelphia, W. B. Saunders Co., 1967, vol. 1, p. 230.

For prompt antibacterial levels in blood and urine: Effective antibacterial levels of Gantanol in both blood and urine are established in from 2 to 3 hours after initial 2-Gm adult dose.

When susceptible urinary bacterial invaders are identified in nonobstructed cystitis and pyelonephritis, Gantanol (sulfamethoxazole) is a logical choice. It controls susceptible *E. coli*, the most common pathogen in acute urinary tract infections, and is also highly effective against other susceptible bacteria most often implicated: *Klebsiella-Aerobacter*, *Staph. aureus* and *Proteus mirabilis*.

For around-the-clock coverage: Each subsequent 1-Gm dose offers up to 12 hours of antibacterial activity. This is especially important during the night, when urinary retention favors bacterial proliferation. A *r.i.d.* dosage schedule is recommended for more severe infections.

For efficacy in nonobstructed acute, chronic and recurrent cystitis and pyelonephritis, when due to susceptible organisms: Gantanol Tablets or pleasant-tasting Suspension can provide your patients with the dependable antibacterial action they need. However, the usual precautions in sulfonamide therapy should be observed, including maintenance of adequate fluid intake, frequent c.b.c.'s and urinalyses with microscopic examination. Common side effects include nausea, vomiting and diarrhea. (It should also be noted that the increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents including sulfonamides, especially in chronic or recurrent u.t.i.)

Before prescribing, please consult complete product information, a summary of which follows:
Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. *Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add amphotericin acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.
Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.
Adverse Reactions: Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin

eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastro-intestinal reactions* (nausea, emesis, abdominal pain, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some gonitogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).
Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.*, depending on severity of infection.
Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.
Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

Correct answers to "Puzzling Pairs" quiz.

- (A) *Candida albicans*. Note budding and variation in size of daughter spores.
(B) RBC. Note central portion representing characteristic concavity of RBC.
- (A) Polymorphonuclear leucocytes. Note partially obscured lobulated nucleus and irregular granules.
(B) Ragweed. Note geometric knobby protrusions of the ragweed particle.
- (A) *Necator americanus* (larval form). Note distinctive head and details of internal organs.
(B) Convulsed cast. Note diffuse fine granular appearance throughout and corkscrew shape of terminal portion.
- (A) *Entamoeba histolytica*. Note chromatoidal bodies.
(B) Histocyte. Note phagocytic vacuoles.

In nonobstructed cystitis due to susceptible organisms

Gantanol® (sulfamethoxazole) B.I.D. Basic Therapy



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N. J. 07110

Medical Tribune

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and Medical News

Vol. 14, No. 7

world news of medicine and its practice—fast, accurate, complete

Wednesday, February 21, 1973

1974 Federal Budget Proposals

4 Major Health Programs Are Set to Be Terminated

Medical Tribune Report

WASHINGTON—Four of the country's major health programs will be terminated under the provisions of the Federal budget for fiscal 1974 that has been presented to Congress by the Nixon Administration.

If the new budget is approved, the Hill-Burton program of hospital construction and renovation as well as the Regional Medical Programs will come to an end in June. Federal support for all biomedical research training grants and fellowships provided by the National Institutes of Health, and for the Community Mental Health Centers program, will be phased out as soon as existing commitments are honored.

Additionally, sizable cuts will be made in the amount of Federal money available as "institutional assistance" to schools that prepare health professionals and nurses, along with a reduction in student aid.

Capitation payments will be continued only for schools of medicine, osteopathy, and dentistry. No direct funds whatsoever will be allocated in 1974 to public health and allied health schools or to their students.

Changes with direct impact on medical practice include an increase in funds to set up a national network of professional

Budget Cuts at a Glance

Medical Tribune Report

Here are the proposed budget cuts at a glance.

- Termination by July 1 of:
 - Hill-Burton program of hospital construction and renovation.
 - Regional Medical Programs.
- Phasing out as soon as possible of Federal support for:
 - All research training grants and fellowships from National Institutes of Health.
 - Community Mental Health Centers program.
- Reduction by \$58,000,000 of funds for training health manpower.

standards review organizations. Costs of Medicaid are to be reduced via a stronger utilization review system. Medicare beneficiaries will pay a bigger personal share of both hospital charges and physicians' bills.

The proposed 1974 budget would bring over-all spending for health programs through the Department of Health, Education, and Welfare up to a total of \$22.2 billion, or a jump of \$3.38 billion over the estimate for fiscal 1973.

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Fetus Photographed



Photograph, made by Dr. Valenti, of left hand of 17-week-old fetus in utero.

Fetal Skin, Blood Taken at 4 Months In Amniocentesis

Medical Tribune Report

SARASOTA, FLA.—Dr. Carlo Valenti of New York, who enjoys the advantage of studying amniocentesis in a state with virtually unlimited abortion, reported here that he has shown the feasibility of extracting both skin and blood from the 16-18-week fetus, using for his trials women who are about to undergo abortion at Downstate Medical Center, Brooklyn.

Dr. Valenti came to the meeting of the

Continued on page 30/34

Survival Data Sifted

Use of Steroids In Shock Stirs 3-Way Debate

Medical Tribune Report

PHILADELPHIA—How solid is the evidence from actual clinical studies that corticosteroids should be used to treat the patient in shock?

This question was answered in three different ways at a symposium here on "Corticosteroids in the Therapy of Circulatory Shock," held by the Philadelphia Physiological Society and the Department of Pharmacology of the Medical College of Pennsylvania.

Three leading investigators—an advocate of the therapy, a skeptic, and one who described himself as a middle-of-the-roader—took part in a panel discussion of data now emerging from laboratories and hospitals. While all three agreed on the solidity and impressiveness of many animal experiments, they expressed sharply divergent opinions about the weight they would give to findings from clinical studies as currently conducted.

In the view of Dr. Richard C. Lillehei, the University of Minnesota surgeon who has long favored steroid therapy in shock, the experience gained at his medical center clearly indicates that corticosteroids increase survival rates.

One set of figures cited by Dr. Lillehei concerned patients with septic shock caused by gram-negative organisms. Of 300 patients treated according to conventional regimens, he said, less than 40 per cent survived. Among 52 patients who ad-

Continued on page 23/27

High Esophageal Cancer Rate In Iran Examined

Medical Tribune World Service

TEHRAN—The extraordinary high incidence of esophageal cancer in the Caspian Sea area is the target of a two-nation research project here.

Data from a cancer registry begun five years ago in two Iranian provinces, Mazandaran and Gilan, show an unusual distribution of the disease. In parts of Mazandaran it is among the highest in the world, with one northeast Mazandaran community, for example, reporting an incidence of esophageal cancer that is 50 times higher than that in England and Wales. In the southern and eastern parts of the same province, however, it is considerably less frequent, and in western Gilan it is comparatively rare.

The research teams include investigators from the French International Agency for Cancer Research and a multidisciplinary group of Iranian scientists.

Continued on page 9

Study of Mouse Utopia: Trouble in Paradise

Medical Tribune Report

POOLESVILLE, MD.—The mouse race, even in utopia, can be as lethal as any rat race, a four-and-a-half-year-old experiment at the National Institute of Mental Health has demonstrated.

In the experiment, conducted by John B. Calhoun, Ph.D., and associates in the Section for Research on Behavioral Systems here, an "ideal" mouse universe was designed, capable of comfortably housing as many as 4,000 animals. This environment, approximately 10 feet square and 4½ feet high, provided optimum conditions of food and water supply, shelter, and temperature, as well as freedom from disease and predators.

Into this Eden Dr. Calhoun placed four breeding couples, which flourished, raised families, and began a disease-free animal colony.

After two years, however, there was clearly trouble in paradise, with a population that had already peaked out at only 2,200 mice, and two and a half years later the colony was extinct, a victim of social disintegration that included a striking loss of interest in sex.

Dr. Calhoun began his explanation of what went wrong with a description of the environment: it consisted of 256 "apartments," or nesting facilities, in four tiers around the walls, "just like a high-rise," with food and water available in cafeterias. Status and wealth consisted of possession of lower-level nesting space, which carried easier access to food and water.

Continued on page 9



Dr. Calhoun standing in the mouse universe at height of the population explosion.

High Tolerance to Alcohol Said to Increase Risk of DTs

Medical Tribune World Service

STOCKHOLM—Some drinkers appear to tolerate large quantities of alcohol over long periods of time without establishing reputations as alcoholics or experiencing social or legal complications.

But a study at Beckomberga Hospital here shows this tolerance is only the tip of the iceberg and that such drinkers face the highest risk of serious mental and physical consequences, particularly delirium tremens.

The study, by Dr. Inna Salum, covered the clinical, chemical, social, and prognostic aspects of delirium tremens and other acute psychiatric sequelae of alcohol abuse in 1,026 male alcoholics treated between November, 1956, and December, 1961.

The patients had been treated on 1,907 occasions in a special ward for acute alcoholic psychoses.

Dr. Salum, who is now with Maria Clinic here, divided her patients into four diagnostic groups. A so-called SB (syndrome B) group consisted of those with tremulous states without psychotic symptoms. An AH (acute hallucinatory) group

contained cases in which, besides tremor, hallucinosis but not disorientation had occurred. Those who had suffered tremor, hallucinosis, and disorientation were placed in a DT (delirium tremens) group. If pseudoposthysteresis (a tendency to retraction of the head and overextension of the back) had also occurred, they were classified in a DT₁ group.

Dr. Salum found that the DT group, and especially the DT₁ group, had on first admission a lower percentage of persons previously treated in a mental hospital for alcohol abuse. The percentage of persons registered for drinking offenses was also lower in the DT group than in the SB and AH groups. It was even lower in the DT₁ group.

Tolerance Tied to Risk

"These differences between the groups suggest a relation between high alcohol tolerance and increased risk of development of delirium tremens," she told MEDICAL TRIBUNE.

She said the frequency of divorced and homeless men, men with impaired working capacity, and men with drinking-offense or criminal records was appreciably higher in the entire test group than in the general population. But the social situation of the DT group was in no respect worse than that of the SB or AH groups.

"Where appreciable differences existed between the groups," she said, "the situation was better in the DT group than in the SB and AH groups."

The number of deaths occurring during the observation period was 275, compared with the expected 77.4. Mortality was 4.1 times as high in the DT group as would be expected in a normal population, and it was 3.0 times as high in the SB and AH groups.

On first admission, 360 patients were classified SB, 206 AH, and 460 DT. About 40 per cent of each first-admission group were readmitted at least once. The total number of admissions and readmissions was 921 in the SB group, 419 in the AH group, and 567 in the DT group.

Dr. Salum said one explanation for the fact that only a small number of alcohol abusers get DTs may be that only comparatively few are able to consume alcohol for such long periods and in such quantities that severe psychiatric and other medical complications can arise.

Method's Accuracy Confirmed

Since 1971, when Dr. Yamamoto began testing the system, he has measured the blood stream velocity in about 100 patients and through diagnosis has confirmed the accuracy of the method.

A drop in the velocity, he said, indicates either an advanced case of arteriosclerosis or congenital degeneration of the retina or retinitis as an aftereffect of toxemia of pregnancy. A jump in velocity is indicative of acute uveitis or inflammation of the iris, choroid, or ciliary body, he added.

The method has the additional advantage of providing a reading in a matter of minutes following eye-drop anesthesia, Dr. Yamamoto said.

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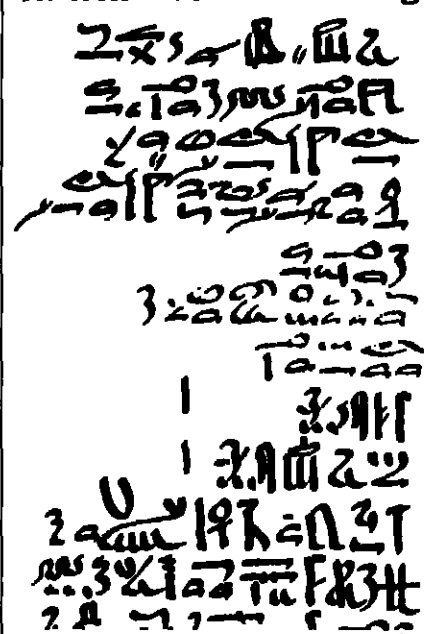
Smoking Halt Speeds Tracheobronchial Clearance

Medical Tribune World Service

STOCKHOLM—With the aid of a radioactive aerosol, a Swedish investigator has demonstrated that tracheobronchial clearance does improve in cigarette smokers who stop smoking.

Dr. Per Camner, of the National Environment Protection Board, studied 17 smokers while they were still smoking, one week after stopping, and three months after stopping. He found that average

Ancient Medical Writing



A section of a fragment of the Ebers papyrus, a collection of Egyptian medical writings that originated in the era of Imhotep. The papyrus, which dates from 1550 B.C., was discovered at Luxor in 1873 by Georg Ebers and is now preserved at the U. of Leipzig.

Australia Would Reduce Number Of Eligible Asian-Trained MDs

Medical Tribune World Service

SYDNEY, AUSTRALIA—Changes in the Medical Practitioners' Act here will reduce the number of Asian-trained doctors eligible for immediate registration for practice in New South Wales.

The act has been amended to exclude a number of Asian universities and medical schools from the list of institutions whose graduates are granted automatic registration. The graduates from the excluded universities—some among Asia's largest—will now have to serve 12 months' probation and then sit for a qualifying examination before setting up practice.

The affected universities include those of Ceylon, Bombay, Rangoon, Calcutta, Madras, Karachi, Lucknow, Dacca, and Agra.

A spokesman for the Medical Registration Board said here that the legislation did not amount to a blanket ban on the institutions. Each application would be treated on its merits.

In 1971, 299 Asians comprised one-third of all graduates to whom registration was granted in New South Wales.

values were about the same on the first two occasions but that after three months, tracheobronchial clearance was significantly more rapid.

Clearance was measured with the aid of a test aerosol of 6-micron monodispersed Teflon particles tagged with technetium-99m.

Dr. Camner's findings were reported to the annual meeting of the Swedish Medical Society here.

Revealing Fetal Sex Might Cause Couple To Choose Abortion

Medical Tribune World Service

JERUSALEM—The prospect of a world in which men would outnumber women by three to one emerged during a round-table discussion by scientists attending the Jerusalem Chromosome Conference.

The discussion was opened by a question raised from the floor: Should the sex of the fetus be revealed to the parents on request if there is no valid medical reason to interrupt the pregnancy?

The speaker himself said No, for if the sex were female, the parents might decide to abort the fetus, hoping that the next pregnancy might produce a boy.

Soon, other speakers predicted, "commercial amniocentesis institutions" will be available, and they will reveal the sex for a fee.

"Abortion on Demand" Cited

And in most Western countries, the tendency towards "abortion on demand" is already a factor or soon will be a fact.

Therefore, the ratio of male to female babies will change drastically within a generation as parents decide the sex of their offspring, some discussants predicted.

Does the medical profession or any other have any right, legal or ethical, to interfere with the sex selection by the parents?

"Why should we interfere?" one of the geneticists said. "It is all for the best. This is one of the most effective ways devised to control the population explosion. We should think twice before we even think of interfering in the process of 'different' sex abortion."

Prof. Cyril Dean Darlington, of the Botany School, Oxford, England, commented: "Let us first see how this experiment works on a 'Pitcairn Island.' From this we can see what will be the face of a society where there are three males vying for the favors of one woman; then we can see how much homosexuality develops."

South Koreans Announce Plans To Reduce Population Growth

Medical Tribune World Service

SEOUL—The South Korean Government is out to reduce population growth to 1.5 per cent by 1976 and to 1 per cent by 1981.

At a ceremony here to mark the completion of the first decade of family planning programs, Health-Social Affairs Minister Lee Kyung-ho reported that the growth rate dropped from 3 per cent in 1960 to 2 per cent in 1970.

During the 10 years, he said, more than 2,000,000 women received IUDs, 160,000 men had vasectomies, and 160,000 additional persons were supplied with pills, condoms, and other means of contraception.

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Caffeine Absolved of Blame For Coffee-Infarction Link

Medical Tribune Report

BOSTON—An association between heavy coffee consumption and acute myocardial infarction, disclosed in a study by the Boston Collaborative Drug Surveillance Program (BCDSP), may be due to "a substance or substances in coffee other than caffeine," according to the investigators.

Another possible explanation, said Drs. Hershel Jick and Dennis Slone, codirectors of the BCDSP and Associate Professors of Medicine at Boston University School of Medicine, "is that patients who drink heavily and patients who develop myocardial infarction have similar personalities, and thus coffee drinking would only be indirectly related to myocardial infarction. We have no information for or against this hypothesis."

Their observations, they said, warrant a re-evaluation of the possible role of coffee drinking in the etiology of acute myocardial infarction.

Two Groups Compared

Their study compared 267 patients who suffered acute myocardial infarction with 1,104 other patients. The groups were matched for age, sex, and the hospital in which they were treated.

It was found that the infarction group drank more coffee than the controls. The data further suggested that "people drinking more than five cups of coffee per day have about twice as great a risk of having acute myocardial infarction as people drinking no coffee at all."

The study, which was reported in *Lancet*, found no significant difference between the two groups studied with respect to tea consumption, and thus caffeine and sugar were ruled out as explanations for the observed association between heavy coffee drinking and acute myocardial infarction.

"Coffee ingestion and cigarette smoking

ECTOPIC BEAT

"As of January 1, 1973, the Speech and Hearing Department of St. Francis Hospital will be known as the Department of Communications Disorders."—release from St. Francis Hospital (Poughkeepsie, N.Y.).

And that's the way things go, these days.
(Regular beat: *Immateria Medica*, pp. 31/35).



Codirectors of BCDSP, Drs. Jick, Slone, and another, examine data taken from U.S., Canada, Europe, New Zealand, and Israel.

Patient Death: N.Y. State MDs Endorse Rights

Medical Tribune Report

LAKE SUCCESS, N.Y.—The Council of the Medical Society of the State of New York has formally endorsed a patient's right, in cooperation with his physician, to decide whether extraordinary means should be employed to prolong his life.

The 23-man governing body, which establishes norms of practice for 27,000 member physicians between annual meetings of the house of delegates, approved a statement submitted by the committee on ethics, chaired by Dr. Joseph G. Zimring of Long Beach, N.Y.

"The use of euthanasia is not in the province of the physician. The right to die with dignity, or the cessation of the employment of extraordinary means to prolong the life of the body when there is irrefutable evidence that biological death is inevitable, is the decision of the patient and/or the immediate family with the approval of the family physician."

Followed "Bill of Rights"

The statement was made public following the issuance of a patients' "Bill of Rights" by the American Hospital Association.

The A.H.A. proposes, among other "rights," that "the patient has the right to receive from his physician information necessary to give informed consent prior to the start of any procedure and/or treatment" and that "the patient has the right to refuse treatment to the extent permitted by law and to be informed of the medical consequences of his action."

Dr. Henry I. Fineberg, executive vice-president of the state society, believes that his organization's statement is a superior guideline for physicians on the issue.

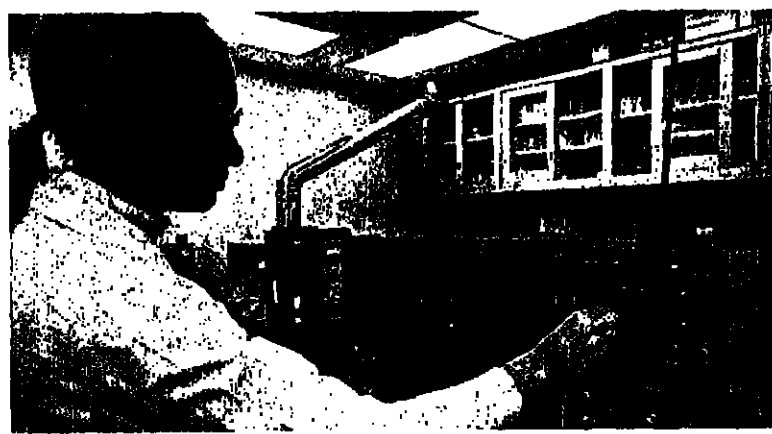
"Under the A.H.A. 'Bill of Rights,' if you wish to interpret it broadly, a seriously ill person suffering from curable depression could withhold consent prior to a procedure which could save his life," he said. "Our councilors thought that the phrase 'irrefutable evidence that biological death is inevitable,' provides a proper safeguard."

Dr. Fineberg said he thinks the New York organization is the first state medical society to put forth such an opinion.

Health Maintenance Through Aerobics Exercise



The Health Watch Plan is a health maintenance program at the Pacific Medical Center in San Francisco with a goal of predictive medicine through the establishment of an individual profile made when the patient is in perfect health. The plan is combined with an aerobic exercise program to measure the body's response to controlled exercise, says Dr. George Williams, plan director. Left, a potential participant in the plan is examined by Dr. Harold Mielke, Jr. Right, weekly blood samples that have been taken from the 50 participants are tested by research technician Inara Kuck.



A daily one-mile run is part of the aerobic regimen. Dr. Joan Ulyot, second from left, leads aerobic exercise groups.

In acute gonorrhea

(urethritis, cervicitis, proctitis when due to susceptible strains of *N. gonorrhoeae*)

Trobicin®

sterile spectinomycin hydrochloride, Upjohn
single-dose intramuscular treatment



High cure rate: 96% of 571 males, 95% of 294 females
(Dosages, sites of infection, and criteria for diagnosis and cure are defined below.)**

Assurance of a single-dose, physician-controlled treatment schedule

No allergic reactions occurred in patients with an alleged history of penicillin sensitivity when treated with Trobicin, although penicillin antibody studies were not performed

Active against most strains of *Neisseria gonorrhoeae* in vitro (M.I.C. 7.5-20 mcg/ml)

A single two-gram injection produces peak serum concentrations averaging about 100 mcg/ml in one hour (average serum concentrations of 15 mcg/ml present 8 hours after dosing)

*Data compiled from reports of 14 investigators.

**Diagnosis was confirmed by cultural identification of *N. gonorrhoeae* on Thayer-Martin media in all patients. Criteria for cure: negative culture after at least 2 days post-treatment in males and at least 7 days post-treatment in females. Any positive culture obtained post-treatment was considered evidence of treatment failure even though the follow-up period might have been less than the periods cited above under "criteria for cure" except when the investigator determined that reinfection through additional sexual contacts was likely. Such cases were judged to be reinfections rather than relapses or failures. These cases were regarded as non-evaluable and were not included.

©1972 The Upjohn Company

Sterile Trobicin®
(spectinomycin hydrochloride, Upjohn)
—For intramuscular injection.
2 gm vials containing 5 ml when reconstituted with diluent; 4 gm vials containing 10 ml when reconstituted with diluent.

An aminocyclitol antibiotic active in vitro against most strains of *Neisseria gonorrhoeae* (MIC 7.5 to 20 mcg/ml). Definitive in vitro studies have shown no cross resistance of *N. gonorrhoeae* between Trobicin and penicillin.

Indications: Acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *N. gonorrhoeae*.

Contraindications: Contraindicated in patients previously found hypersensitive to Trobicin. Not indicated for the treatment of syphilis.

Warnings: Antibiotics used to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Patients should be carefully examined and monthly serological follow-up for at least 3 months should be instituted if the diagnosis of syphilis is suspected. Safety for use in infants, children, and pregnant women has not been established.

Precautions: The usual precautions should be observed with atopic individuals. Clinical effectiveness should be monitored to detect evidence of development of resistance of *N. gonorrhoeae*.

Adverse reactions: The following reactions were observed during the single-dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia.

During multiple-dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single and multiple-dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.

Dosage and administration: Keep at 25°C and use within 24 hours after reconstitution with diluent.

Male:—single 2 gram dose (5 ml), intramuscularly. Patients with gonorrheal proctitis and patients being re-treated after failure of previous antibiotic therapy should receive 4 grams (10 ml). In geographic areas where antibiotic

resistance is known to be prevalent, initial treatment with 4 grams (10 ml) intramuscularly is preferred.

Female:—single 4 gram dose (10 ml) intramuscularly.

How supplied: Vials, 2 and 4 grams—each with ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.9% w/v. Reconstitution yields 5 and 10 ml respectively with a concentration of spectinomycin dihydrochloride pentahydrate equivalent to 400 mg spectinomycin per ml. For intramuscular use only.

Susceptibility Powder:—for testing in vitro susceptibility of *N. gonorrhoeae*.

Human pharmacology: Rapidly absorbed after intramuscular injection. A two-gram injection produces peak serum concentrations averaging about 100 mcg/ml at one hour with 15 mcg/ml at 8 hours. A four-gram injection produces peak serum concentration averaging 160 mcg/ml at two hours with 31 mcg/ml at 8 hours.

For additional product information, see your Upjohn representative or consult the package insert.

Upjohn
The Upjohn Company, Kalamazoo, Michigan 49001

Drug Use Seen Altering Status Of Psychiatry

Medical Tribune Report

NEW YORK—Psychiatry is on the move "back into general medicine" as a result of the "great impact" of psychotherapeutic drugs over the past 20 years, according to a panel of experts in a televised, transatlantic seminar.

Two main developments responsible, according to the three British and two American participants, were the use of long-acting, antipsychotic injections in maintaining schizophrenics in the communities and of lithium in the treatment of manic states.

The closed-circuit workshop allowed professional audiences in 10 American cities to question Drs. W. Linford Rees, Norman W. Immlah, and Malcolm H. Lader in London, as well as Dr. Sidney Mallat and the program's chairman, Dr. Leo E. Hollister, in New York. The discussion, "Recent Advances in Psychotherapeutic Drugs," was sponsored by the American Psychiatric Association and the Royal College of Psychiatrists.

In assessing the impact of psychotherapeutic drugs, Dr. Mallat, deputy director, New York State Psychiatric Institute, and Professor of Psychiatry and vice-chairman of the department, Columbia University College of Physicians and Surgeons, said, "I have seen the practice of psychiatry altered irrevocably in a direction which is beneficial, I think, to patients as a whole."

Belongs in General Medicine

Dr. Lader, of the Institute of Psychiatry, University of London, observed that "the impact of the psychotropic drugs has been to put psychiatry back into general medicine—where I, personally, feel it belongs."

"We are seeing policies in this country," Dr. Lader said, "in which the large area mental hospital now is regarded as having outlived its function and the treatment of the acute patient, at any rate, is being put back into the acute general hospital in the community." In contrast, 20 years ago, under the influence of psychoanalysis and the geographic isolation of most mental hospitals, "there was a tendency for psychiatry to become more and more alienated from the rest of general medicine."

Today in Great Britain, according to the panel, the majority of cases of depressive illness are being treated by general practitioners rather than psychiatrists. "It has been estimated that only one in 200 depressed patients are referred to psychiatric clinics," said Dr. Rees, Professor of Psychiatry, University of London, and physician-in-charge, St. Bartholomew's Hospital, London.

Reviewing the introduction of various psychotropic drugs since the early 1950s, Dr. Rees commented that "the phenothiazines still hold pride of place in the treatment of acute and chronic schizophrenia and are also useful in the management of disturbed and overactive behavior in organic mental states, both acute and chronic, in the dementias and in overactivity in children and mentally subnormal patients."

Community Care "Revolutionized"

Among the phenothiazines, Dr. Rees noted the importance of fluphenazine enanthate and, especially, fluphenazine decanoate, which have, he said, "in fact revolutionized the community care of patients suffering schizophrenia."

Dr. Immlah, Clinical Lecturer in Psychiatry at Birmingham University, agreed that the transition from mental to general hospital treatment of psychiatric disorders is one of the most significant effects of psychopharmacologic developments. He added, however: "I think we must give increasing attention to what we are going to do with patients in the community."

What's new and important in rheumatology?—II

The Consultant

Dr. LEE E. BARTHOLOMEW

Professor of Rheumatology,
Head, Division of Rheumatology,
Albany Medical College, Union University, Albany, N. Y.



What are the current concepts of the immunologic aspects and treatment of lupus erythematosus?

Systemic lupus erythematosus (SLE) is the prototype of immune complex diseases. Identification of specific antigen-antibody complexes in the glomeruli of patients with lupus and with the discovery of fixation of complement in the process has greatly added to our knowledge of the pathogenesis of this disease. For reasons as yet unknown, this particular antigen-antibody (DNA-anti-DNA) complex appears to be caught in the glomerular basement membrane and is not filtered as some other complexes are. With the fixation of complement and the release of the chemotactic and other biologically active principles, the influx of leukocytes occurs and their final breakdown and release

"Identification of specific antigen-antibody complexes... has greatly added to our knowledge..."

of lysosomal enzymes is apparently responsible for at least part of the inflammation and destruction of the kidneys. It is obvious that many other antigen-antibody reactions are occurring in this disease, and these are being studied. It appears that, in many cases of active lupus nephritis, as DNA antibody diminishes the nephritis improves and the serum complement levels rise. For this reason, patients who have low serum complement levels should be followed regularly with this test and treatment judged according to the level of complement. However, there are a small number of patients who continue to have lowered serum complement levels whose nephritis and other evidence of activity of their systemic lupus is under good control. There is evidence that both involved and normal-appearing skin of patients with SLE have deposits of gamma globulins in the basal cell layers. This provides an additional diagnostic measure. Vasculitis presumably is in part an immune reaction, and there is recent evidence that central nervous system lupus is associated with a very low hemolytic C4 component of complement.

Diagnostically, certainly fluorescent antinuclear antibody tests, with their appropriate patterns, and the titer if possible, are important. Positive LE preps occur with positive antinuclear antibody (ANA) tests, but if the ANA is negative there is no reason to order LE preparation. Under current study in various laboratories, and soon to be available routinely, are more sensitive methods for the various antinuclear antibodies, such as DNA-binding, RNA-binding methods, hemagglutination

"Current interest in the use of the cytotoxic agents is well founded..."

and complement fixation tests using purified nuclear antigens. Biopsies of both normal and involved skin with fluorescent studies are important, and probably most patients should have renal biopsies with fluorescent studies in addition to routine pathologic studies.

Treatment of systemic lupus continues to revolve around the steroids as the most important agent. It is hard to make any firm statements as to which patients should

have high doses and which patients should have moderate doses of steroids. In general, patients who have diffuse proliferative glomerulonephritis have the poorest prognosis and probably should be treated most aggressively with high doses of steroids in the 60-100-mg. range daily. Patients with focal nephritis and with membranous nephritis have better prognoses and probably can be handled with lower doses of steroids, starting with approximately 30 mg. of prednisone daily. Patients should be started on daily therapy until all evidence of activity of their disease has subsided, including normalization of their sedimentation rate and serum com-

plement levels and the return of the leukopenia to normal, correction of their anemia, etc. At that time, if the patient is under good control, alternate-day therapy can be started. In general, I add antimalarial preparations to those patients with lupus, particularly those with skin lesions or arthralgias. Hydroxychloroquine, in doses of 200 mg. twice daily, is usually started. These patients should have careful ophthalmologic examinations before starting the therapy and at every four to six months while on treatment, and if significant changes are found in the fundi the drug should be stopped and the patient continued to be watched. In addition, I usually use therapeutic doses of salicylates, particularly if arthritis and arthralgias are present.

The current interest in the use of the cytotoxic agents is well founded in terms of controlled studies. It is apparent that azathioprine, cyclophosphamide, and other drugs are effective. They work both as anti-inflammatory agents and certainly cyclophosphamide as an immunosuppressive agent. I personally do not use these drugs routinely, but in severe cases—particularly those with nephritis—I always consider adding them early in the course of their disease. These drugs have not been accepted by the FDA for treatment in these diseases, so that each case has to be

Next in Consultation

DR. T. ALBERT FARMER, JR., Dean, University of Tennessee College of Medicine, Memphis.

... will answer such questions as:

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- What's new in continuing education? for physicians in practice?

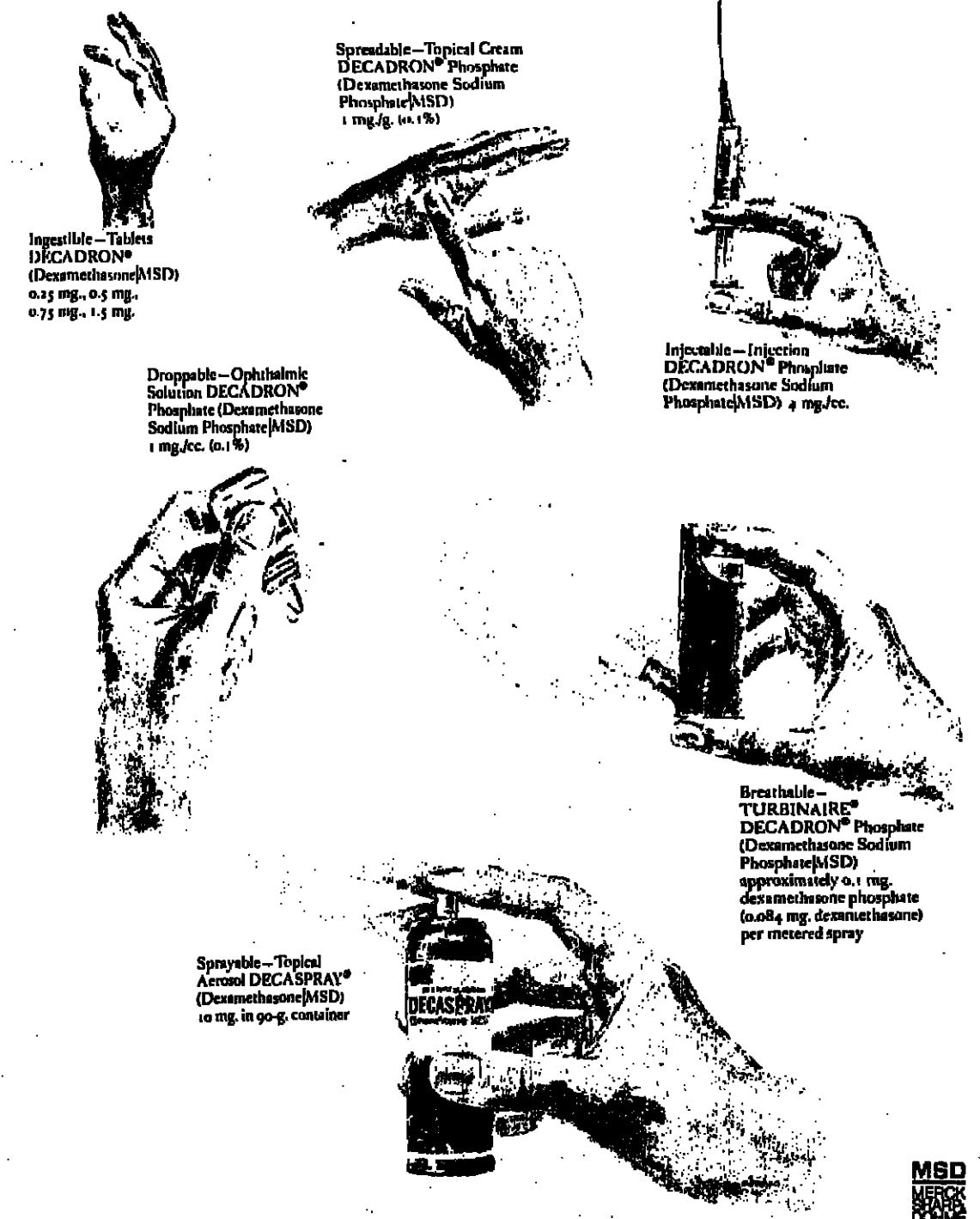
considered on its own merits and both patient and physician be aware of the potential toxicity and long-term problems. I feel that caution should be used in the use of these drugs. There is evidence already that long-term doses of cytotoxic agents may increase the frequency of certain tumors, particularly the lymphomas of reticulum cell sarcoma type.

After the disease is under control, the steroids are gradually decreased but should not be discontinued for long periods of time. One of the great problems in lupus is to decrease steroids too rapidly. The disease will flare, and with each flare it is often more difficult to control the disease.

In some cases the steroids have been withdrawn, and patients have been continued on the antimalarial drugs for several years without evidence of flares.

See related story on page 27.

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Psychologist Links Criminality to Heredity

Medical Tribune Report
WASHINGTON—Do hereditary factors contribute to criminality?

The answer is probably Yes, a leading psychologist said here at a symposium held by the American Society of Criminology during the annual meeting of the American Association for the Advancement of Science.

David Rosenthal, Ph.D., who heads the laboratory of psychology at the National Institute of Mental Health, carefully qualified this view by stressing that sociocultural factors are primary in criminal behavior. He also emphasized that definitions of crime vary from state to state and country to country.

But when the mass of pro-and-con evidence on genetic elements has been weighed, he said, "it is difficult not to come to the conclusion that heredity plays some role in both psychopathy and criminality."

Findings cited as relevant by Dr. Rosenthal are those emerging from studies of twins and of adopted children.

Types of Twins Compared

By the first research strategy, he pointed out, genetically identical twins are compared with same-sex fraternal twins who share only about half their genes in common. By the second, adopted persons having marked personality disorders or arrest records are compared with control subjects—other adopted persons closely matched for age, sex, social class, and age at which adoption took place.

Nine studies of criminality and psychopathic personality in twins have been conducted in different parts of the world over the past four decades, Dr. Rosenthal said. Without exception, the concordance rate for monozygotic twins is higher than the concordance rate for dizygotic twins.

To obtain a general estimate of the levels of concordance represented, Dr. Rosenthal combined the different sets of data, even though he cautioned that the resulting figures cannot be considered scientifically valid because of differences in sampling procedures, cultural climates, and criminal laws.

The nine studies included 219 pairs of monozygotic twins, of which slightly more than 50 per cent were concordant for psychopathy or criminality. By contrast, the concordance rate for 282 pairs of dizygotic twins was about 20 per cent.

Dr. Rosenthal called these findings "consistent with a genetic hypothesis regarding psychopathy and criminality" but pointed out that possible environmental factors could also explain the observations.

Two adoption studies reported in 1972 have provided a more precise way of separating nature-nurture variables, he said.

In Denmark, an investigation conducted by Dr. P. Schulsinger was based on an adoption register that included approximately 5,500 persons who had been given up for nonfamily adoption at an early age between 1924 and 1947. Of this total, 507 were found to have either a history of admission to a psychiatric facility or a police record, and among them were 57 persons diagnosed as psychopaths according to strict criteria.

Controls Various Matched

The 57 controls—selected from the remaining 5,000 adoptees with no history of psychiatric contact—were matched for age, sex, social class, and, in many instances, neighborhood of rearing and age of transfer to the adopting family.

Case records of the biologic and adoptive relatives of all 114 persons were then examined by the investigator (while "blind" about the group to which each subject belonged) to determine the frequency of psychopathic disorder in groups.

The frequency of diagnosed psychopathy in the biologic relatives of the 57 index cases proved to be about two and one-half times greater than the frequency among biologic relatives of the control subjects, Dr. Rosenthal said. Furthermore, a similar difference was found in the frequency of what the investigator termed a "spectrum of psychopathic disorders": personality

disorders, observation for psychopathy or probable psychopathy, character deviation, and such conditions as criminality, alcoholism, or drug abuse.

In all instances, the frequency of the disorders in the adoptive relatives was similar to the findings in the biologic relatives of the control subjects.

"It is difficult to find any environmental explanation for these findings," Dr. Rosenthal commented, "and, indeed, I would be inclined to suggest that this is the first body of evidence to make such a compelling case for the genetic hypothesis with regard to psychopathy."

The NIMH investigator also cited a study reported by Dr. Raymond R. Crowe, of the University of Iowa (MEDICAL TRIBUNE, January 3), in which 52 persons who had been born to inmates of a women's reformatory and given up for adoption were compared to 52 control subjects matched for age, sex, race, and approximate age at time of the adoptive decree. About 90 per cent of the criminal mothers were felons.

Among the index cases, eight had arrest records, with a total of 18 arrests, and seven had received convictions. Among the controls, only two had arrest records,

for a total of two arrests, and one had been convicted. The study revealed a tendency for the type of crime committed by mother and child to be of a similar nature.

Variables Tied to Criminality

Dr. Rosenthal repeatedly stated that in discussing the role of heredity in criminality "we are not talking about a specific gene with a specific locus and specific discernible biological defects." But he pointed out that the following genetically influenced variables are "probably associated in some degree" with criminality:

Electroencephalographic abnormalities, low intelligence, mesomorphic body build, psychotic or near-psychotic personality, chromosomal aneuploidy, alcoholism, sexual disturbances, the hyperkinetic syndrome, and emotional instability leading to drug addiction.

"The implication of a genetic basis underlying some criminality does not mean that an individual harboring the genotype must at some time commit a crime," he declared. "My own opinion is that most crime arises because of environmental and psychological influences, and that sociocultural factors in modern society primarily underlie the great current crime wave."

Ca Induction Explored



New methods of inducing cancer in animals are being explored, part of investigations seeking an ideal model for the study of pancreatic cancer. At U. of Kansas Medical Center Dr. J. J. Reddy, Assistant Professor of Pathology, prepares guinea pigs for injection.

Screening for Lead Content



Cleveland's first comprehensive Childhood Lead Poisoning Control Program gets nobly under way as field inspector William Morrison draws blood sample from youngster at the Thomas McCafferty Health Center, one of eight screening centers set up in the Cleveland area. At least 5,000 children will be screened for high lead content during the first year of the five-year program.

Liver Disease May Predispose To Adult Respiratory Distress

Medical Tribune Report

PHOENIX, ARIZ.—Patients with liver disease are predisposed to the adult respiratory distress syndrome, a Phoenix investigator cautioned here.

Dr. Brendon Thomson, of the Phoenix Indian Medical Center, reported eight cases seen in one year in which both disorders were identified. The sole survivor had "clinical findings compatible with viral hepatitis," and liver disease in the other patients was confirmed at autopsy. Alcoholism was the most common cause of hepatic disease, Dr. Thomson told the Arizona Regional Meeting of the American College of Physicians.

Three of the patients were admitted with dyspnea as the chief complaint. The other five presented with liver disease or infection, with subsequent development of respiratory difficulties. In all cases, tachypnea, tachycardia, and fever were present, and four patients died within 24 hours of admission.

"The major precipitating factor of the adult respiratory distress syndrome was shock or pneumonia," Dr. Thomson said. "Other possible contributing factors were anemia, hypoalbuminemia, cardiac decompensation, fluid overload, coagulation defects, and encephalopathy."

Dr. Donald Sandweiss was coauthor.

Duodenal Anatomy Is Demonstrated By Glucagon With Few Side Effects

Medical Tribune Report

CHICAGO—Double-blind, crossover barium x-ray studies have demonstrated that glucagon temporarily induces an atonic and amotile duodenum and provides a reliable demonstration of duodenal anatomy with

minimal side effects, a team of investigators from Indianapolis reported here.

This medication "should extend the usefulness of hypotonic duodenography," they told the 58th annual meeting of the Radiological Society of North America.

Two Studies Undertaken

In one study, the effects of 2 mg. glucagon and 1 mg. atropine sulfate on duodenal motility and motility were compared with placebo in six asymptomatic cooperative men. In a second, similar study with the same number of subjects, 2 mg. glucagon and 30 mg. propantheline bromide were compared with placebo. All medications were given intramuscularly and all subjects in both studies received all three medications.

Following glucagon there was a significant decrease in duodenal motility and tonicity, in comparison with the placebo, and the radiologist reported a significant response to the drug at 10 and 30 minutes, the investigators said. Response following administration of atropine sulfate and propantheline bromide, compared with placebo, were variable.

The investigators were Drs. Roscoe E. Miller, Stanley M. Chernish, and Bernard D. Rosenak, and B. E. Rodda, Ph.D.

2 Features of Boeing Jet May Be Safety Hazards, According to an Expert

Medical Tribune World Service

MELBOURNE, AUSTRALIA—Two of the passenger attractions of the Boeing 747 Jumbo jet—the staircase leading to the upstairs lounge, and the high ceilings—are safety hazards, according to an American aviation medicine expert.

Dr. John K. Cullen, of Pan American World Airways, addressing the second International Aerospace Medicine Conference here, said:

"From the very inception of the idea of an upstairs lounge, it has been recognized that the spiral staircase with its small treads and steep pitch had to be a hazard, and such has proved to be the case. There have been a great many injuries from falls and a few of these have been serious."

Cites High Ceilings

As to the high ceilings, he explained: "One does not ordinarily think in terms of falling from a ceiling, but when unexpected turbulence is encountered, this is exactly what happens. The unsuspecting passenger or crew member is suddenly thrown upward—often to the maximum height of the ceiling—and then falls to the floor. It follows that the higher the ceiling, the greater the distance the hapless victim will fall and the greater will be the force with which he will strike the floor."

Dr. Cullen reported, however, that a review of the experience of the major airlines using the Jumbo indicated that, overall, there have been fewer in-flight medical emergencies aboard the 747s than aboard smaller jet aircraft.

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INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; intertrigo; androgenic alopecia; chronic infectious dermatitis; stasis dermatitis; pyoderma; necrotic eczema and chronic eczematoid of the vulva; acne vulgaris; localized or disseminated neurodermatitis (lichen simplex chronicus); prurigo; pruritus (vulva, scrotum, anus); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds (lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain. If used under occlusive dressings or for a prolonged period, watch for signs of pillular-adrenal axis suppression. May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of non-susceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reactions occur. Rarely, local corticosteroids may cause atrophy at site of application when used for long periods in intertriginous areas.

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Apply a thin layer to affected areas 3 or 4 times daily.
HOW SUPPLIED
Cream, 5% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 gm. Ointment, 5% Iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 gm. Lotion, 5% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 1 ounce. Mild Ointment, 5% Iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 5 and 1 ounce.

Consult complete product literature before prescribing.

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C I B A

Hand Temperature Rise May Lessen Migraine

Medical Tribune Report
TOPEKA, KANS.—The possibility of relieving migraine headache by using an autogenic feedback training technique to achieve hand temperature control has been suggested by investigators from the Menninger Clinic here.

They defined autogenic feedback training as simultaneous regulation of mental and somatic function, with "desired somatic responses . . . brought about by passive concentration upon phrases of pre-selected words."

Their experimental study, which began in August, 1969, was initiated after an autogenic feedback training research subject, "in training to learn to control brain waves, to reduce electromyographic potential in the forearm musculature, and to increase blood flow in the hands, which is measured by hand-skin temperature," reported a correlation between achieving a rise of 10° F. in hand temperature in a two-minute period with a spontane-

ous recovery from a migraine headache. The study included 75 subjects—63 with migraine headache, 10 with tension headache, and two with cluster headache. Of these, eight dropped out of the study and five entered it too late for development of

sufficient data. The team said they feel that only the migraine sufferers provided a large enough sample for adequate appraisal.

The authors—Dr. Joseph D. Sargent, Elmer E. Green, Ph.D., and E. Dale

Walters—said that "74 per cent of the migraine sufferers were improved. . . . Presently the feeling is that all those subjects who have succeeded in control of headache have developed the ability to increase blood flow in the hands in less than one minute in almost 100 per cent of the situations in which they detect the onset of a headache."

Members of Multiple Sclerosis Unit Named

Medical Tribune Report
WASHINGTON—Elliot L. Richardson, former Secretary of the Department of Health, Education, and Welfare, has invited four members of the National Institutes of Health's National Advisory Neurological Diseases and Stroke Council and five public members to serve on the newly created National Advisory Commission on Multiple Sclerosis.

Charles W. V. Meares, retired chairman of the New York Life Insurance Company, has been asked to head the commission. He is vice-president and a

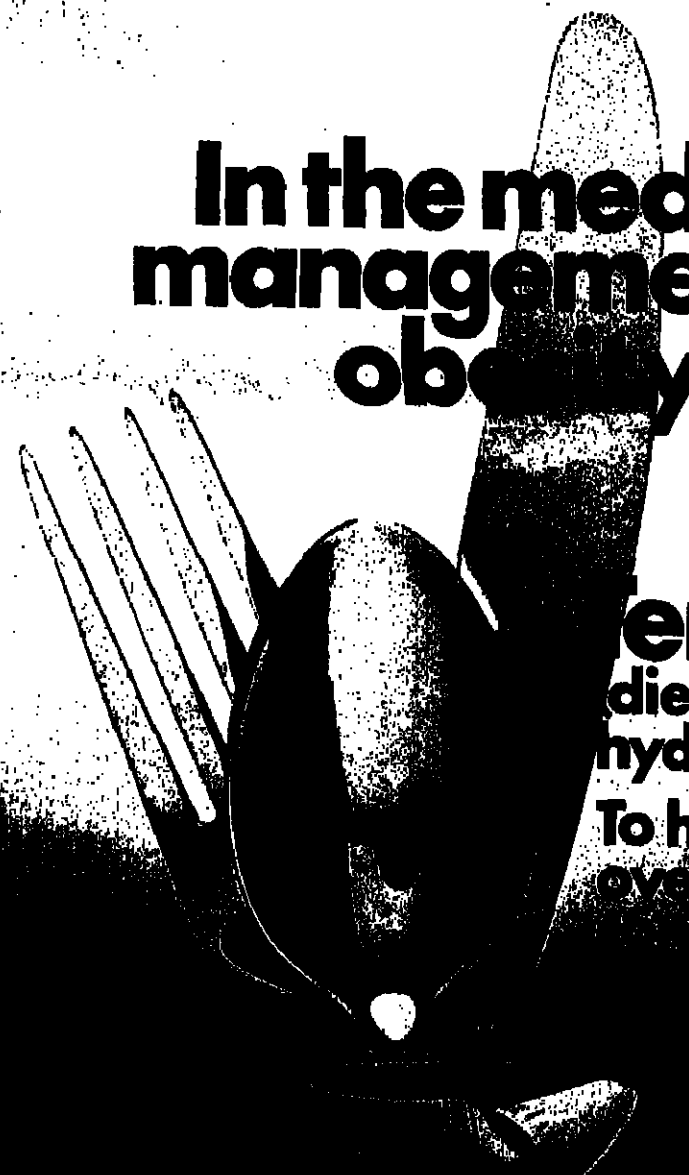
director of the National Multiple Sclerosis Society.

The members of the neurologic diseases and stroke council who were invited to participate on the new commission are Dr. Lyle Albert French, vice-president for health sciences affairs at the University of Minnesota Medical School; Ellen R. Grass, president of the Grass Foundation, Quincy, Mass.; Dr. George B. Koelle, Professor of Pharmacology, and chairman of the department, University of Pennsylvania School of Medicine; and Dr. Richard P. Schmidt, dean of the College of Medi-

cine, Upstate Medical Center, State University of New York, Syracuse.

The public members, in addition to Mr. Meares, invited to serve on the commission are Dr. Stanley M. Aronson, Professor of Medical Science and pathologist-in-chief, Miriam Hospital, Providence, R.I.; Janice Dudley, project director, Neurologic Disease Epidemiologic Study, Seattle; Dr. H. Houston Merritt, dean emeritus, College of Physicians and Surgeons, Columbia University; and Mary Ruffner of Phoenix, Ariz., active in the National Multiple Sclerosis Society.

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"Possibly" effective: Overweight
Final classification of less-than-effective indication requires further investigation

Contraindications: Concurrently with MAO inhibitors. In patients hypersensitive to the drug. In immediately unstable patients susceptible to drug abuse.

Warnings: Use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Usually severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. An is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few patients an increase in convulsive episodes has been reported.

Sympathomimetic cardiovascular effects reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. **Atypical phenomena** reported include such conditions as rash, urticaria, erythema, and erythema. **Gastrointestinal effects** such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. **Specific reports on the hematopoietic system** include two cases of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: Dosage tablets: One 75 mg. continuous release tablet daily, swallowed whole, in midmorning, 25 mg. tablets: One 25 mg. tablet, three times daily, one hour before meals, and in midmorning if desired to overcome night hunger. Use in children under 12 years of age is not recommended.

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Wednesday, February 21, 1973

CURRENT OPINION

By MARVELLA BAYH
Wife of U.S. Sen. Birch Bayh of Indiana

WHEN A WOMAN undergoes breast surgery, even the most loving husband and thoughtful doctor cannot answer all of the questions that run through the patient's mind in the days immediately following the operation. I know. I had a mastectomy in October of 1971.

My husband had spent much of 1971 traveling across the country weighing the possibility of a campaign for the Presidency. When I went into the hospital to undergo preliminary surgery for a biopsy, he suspended his campaign. When the biopsy was positive, he immediately withdrew from the Presidential campaign and provided the love and attention which I needed during the time of greatest physical and mental trauma.

My doctor was wonderful. I have unqualified confidence in him and appreciated his assurances that surgery for breast cancer did not preclude my returning to a completely normal life style. The nurses and the entire hospital staff were just terrific in every way.

But soon I began to ponder the female questions of how my clothes would fit and whether my femininity would somehow be reduced by the surgery. It is about this

"Depression may become a real danger for mastectomy patients."

time that depression may become a real danger for mastectomy patients.

About five or six days after the operation, my hair had lost its set, and I was feeling quite dowdy when an attractive, well-dressed lady entered my room and identified herself as a representative of "Reach to Recovery." I recalled my doctor had told me to expect a visitor from the American Cancer Society who would answer questions I might have about the after-effects of my surgery.

As my visitor began discussing the post-operative exercises which would be most important to my recovery, I noticed that she had a lovely figure and that she was wearing a form-fitting blouse. I thought, "How can she understand the problem which I face?"

To my amazement my visitor mentioned that she, and all other Reach to Recovery volunteers, had undergone a

"How can she understand the problem which I face?"

mastectomy. My reaction to her visit changed immediately. All of a sudden there was someone who could answer all my questions from her own firsthand experience. I realized that what I had been told about regaining my vitality and resuming a normal life style was absolutely true.

In many respects the visit from the Reach to Recovery volunteer was the turning point in my recuperation. Besides lifting my spirits, my visitor provided me with the full range of Reach to Recovery literature and the organization's kit for patients. This includes a ball and rope for exercising and a temporary prosthesis, which I wore home from the hospital looking completely normal. The literature included such important information for mastectomy patients as suggestions for altering clothes for the best fit, the kinds of breast forms available, and, quite importantly, the volunteer's home telephone number in the event a delicate question should arise. Here was someone who not only cared but who fully understood what I was experiencing and was ready and anxious to help me through the period of adjustment.

I subsequently found out that Reach to Recovery had been founded by a mastectomy patient, Teresa Lasser, in 1953 with funds provided by her husband, Mr. Lasser has spent the past 20 years improving and expanding the services of Reach to Recovery, so that it is now providing guidance to mastectomy patients around the

world. Since 1969 the American Cancer Society has funded Reach to Recovery—an important indication of the high regard the organization has earned among those most concerned with the problems of cancer patients.

One hard rule to which Reach to Recovery has adhered is that its volunteers

"Reach for Recovery . . . volunteers will not visit a cancer patient unless called in by the patient's doctor."

will not visit a cancer patient unless called in by the patient's doctor. Thus, despite the truly valuable role which this organization can play, Reach to Recovery is unable to realize its full potential because all doctors do not know about it and some who know of its existence are reluctant to call on Reach to Recovery volunteers because of lack of knowledge about the organization's goals and procedures.

As one who benefited substantially from Reach to Recovery, I would urge all doctors with mastectomy patients to appraise themselves of the services and success of this fine organization. All volunteers are properly briefed before visiting patients; they know what pitfalls to avoid and how



MARVELLA BAYH

to offer guidance in the most constructive manner. The exercise kit and literature are carefully prepared with authoritative medical advice.

Reach to Recovery is not a substitute for high-quality medical care, nor can it replace the treasured support of loved ones during the period of crisis. By limiting its volunteers to those who had had mastectomies, by being candid, by offering literature which has guidance not only for patients but for their husbands and children, by offering hope where there is despair, Reach to Recovery can play a truly significant role in the recovery of women who undergo breast surgery. I know. I've been there.

Role of Amniocentesis Apart From Abortion Is Emphasized

Medical Tribune Report

WASHINGTON—Now that amniocentesis has come of age, physicians ought to stop thinking of it solely in connection with abortion and start thinking of all the normal babies being delivered to women who would not previously have dared to become pregnant after an initial catastrophe.

So said two pioneers in the field, Dr. Cecil Jacobson, of George Washington University, and Dr. Michael M. Kaback, of the University of California at Los Angeles, at separate sessions here of the American Association for the Advancement of Science.

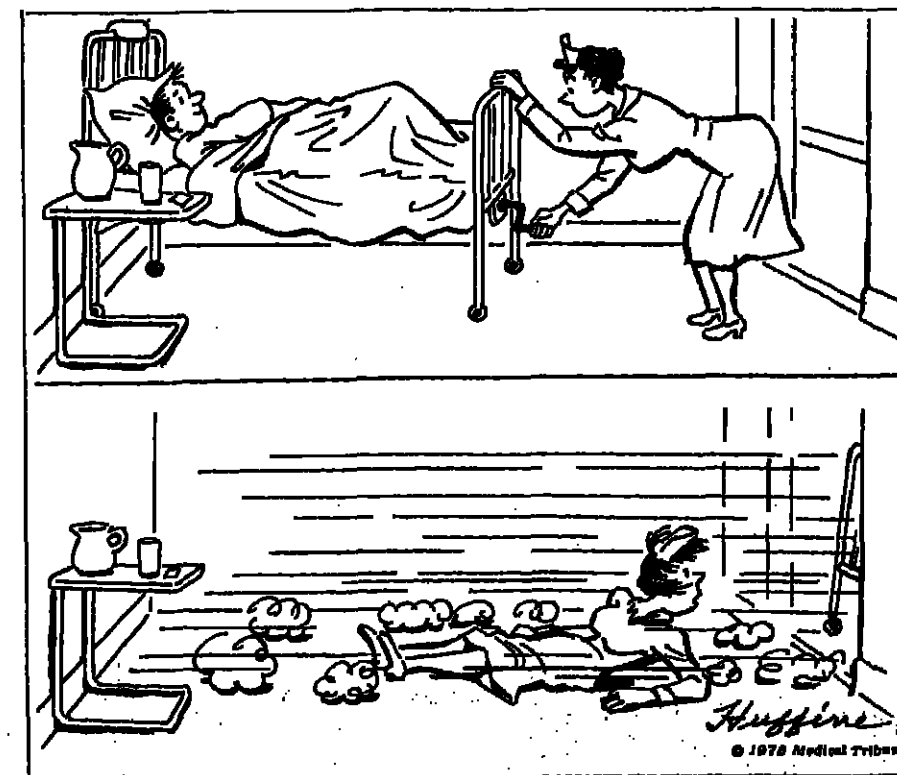
Dr. Jacobson, who performs his taps at the 18th to 20th postmenstrual week, using surgical preparation and usually preliminary ultrasonography to minimize risks, reported: "We have seen no maternal complications in the 557 procedures we have done."

While he has not subjected these cases

to final statistical analysis, he offered the following percentages in cases where there is an affected proband in the family; translocations, 25 per cent of fetuses defective; trisomies, 3-5 per cent; maternal age over 37, 1-2 per cent; X-linked disease and metabolic errors, 25 per cent each; and suspected mutagenic exposure, 2-5 per cent.

In his 270 control cases, where there was no proband to arouse suspicion, he has found two fetuses candidates for abortion, an incidence of less than 0.5 per cent.

Dr. Kaback, who has been compiling figures for all of North America, reported 110 pregnancy terminations following 1,416 amniocenteses. He broke down the terminations as follows: gross chromosomal abnormalities, 77 per cent; metabolic errors, 13 per cent; X-linked defects, 7 per cent; and mutagens, such as viral disease, radiation, drug exposure, 3 per cent.



A Mouse Population In Ideal Community Runs Into Troubles

Continued from page 1

The mice in the upper tiers had to expend more energy on survival, and in this colony "energy was income—the economic factor," Dr. Calhoun told MEDICAL TRIBUNE.

A mouse likes to live in a small group of about a dozen animals, he said. Each group stakes out a territory, and the territory and the females within it are defended by the older males. Within the group, the older mice teach the offspring their appropriate social roles; socialization thus depends on membership in a group.

The first 14 mouse groups that developed from the original settlers—about 150 or so animals—took over the prime living space in the environment. In the absence of disease and predators, a high percentage of their young survived, but in larger and larger numbers they were rejected for group membership because there were so many of them that they began to be perceived as threats by the established groups.

Establishment Males Exhausted

The endless need for defending territory and females from the new males exhausted the establishment males, which began to die off; the new males then aroused aggression in the establishment females, which had to defend themselves, offspring, and territory against the intruders. Unfortunately, this aggression, Dr. Calhoun related, was also turned against the females' own young, which, as a result, received no proper role education. In fact, since the young mice were not being permitted to join groups, the traditional roles were disappearing.

"If society cannot provide enough social roles for its members, violence and aggression are produced. The establishment breaks down, and even the mature mice cannot fulfill their function," Dr. Calhoun pointed out.

The first generations that received no role education were indeed characterized by aggression and violence. The young adult males were sexually assaultive, as they led a "life on the street" on the floor of the "ideal" universe, and the social order began to break down, under the pressure of unstructured population growth, crowding, and lack of privacy.

By the time the colony was two and a half years old, the experimenters could see that the last 1,000 mice born were not aggressive and violent but passive and withdrawn. Many of them refused to leave their individual nests. The investigators labeled them "the beautiful ones," since they were physically perfect specimens with none of the scars of struggle. But they also refused to relate sexually, and that is what doomed the colony.

Breeding stopped. By the beginning of January, the colony had dwindled to one doddering male and 15 doddering females. By the end of the month, the colony was extinct.

Dr. Calhoun and his group have performed the experiment before in smaller utopias and have found that the smaller the utopia, the more rapid its extinction.

They believe that their demonstration of the effects of unstructured population growth and concomitant overcrowding has a lesson for human beings.

Iran's Eye Institute

BALTIMORE—An agreement to help train the staff of a new eye research institute at Iran's Pahlavi University Medical School has been made by the Johns Hopkins Wilmer Ophthalmological Institute.

The proposed 100-bed Reza Pahlavi Eye Institute will be completed in 1973, said Dr. Ali A. Khodadoust, its director and currently a Visiting Professor of Ophthalmology at Johns Hopkins.

the long-range analgesic

in chronic pain: continued relief without risk of tolerance

Though Talwin® Tablets can be compared to codeine in analgesic efficacy, Talwin is not subject to narcotic controls. For patients who require potent analgesia for prolonged periods, Talwin can provide consistent, long-range relief, with fewer of the consequences you've come to expect with narcotic analgesics.

- Comparable to codeine in analgesic efficacy: one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.
- Tolerance not a problem: tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- Dependence rarely a problem: during three years of wide clinical use, only a few cases of dependence have been reported. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.
- Not subject to narcotic controls: convenient to prescribe—day or night—even by phone.
- Generally well tolerated by most patients: infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects may decrease or disappear after the first few doses. (See next page of this advertisement for a complete discussion of Adverse Reactions and a Brief Summary of other Prescribing Information.)

50mg. Tablets **Talwin®**
brand of
pentazocine
(as hydrochloride)
in moderate to severe pain

in chronic pain: continued relief without risk of tolerance

Talwin® Tablets brand of pentazocine (as hydrochloride)
Analgesic for Oral Use—Brief Summary

Indications: For the relief of moderate to severe pain.

Contraindication: Talwin should not be administered to patients who are hypersensitive to it.

Warnings: Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Head Injury and Increased Intracranial Pressure. The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: Certain Respiratory Conditions. Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously given narcotics, including methadone for the daily treatment of narcotic dependence, have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include gastrointestinal: nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. CNS effects: dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see Acute CNS Manifestations under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. Autonomic: sweating; infrequently flushing; and rarely chills. Allergic: infrequently rash; and rarely urticaria, edema of the face. Cardiovascular: infrequently decrease in blood pressure, tachycardia. Other: rarely respiratory depression, urinary retention.

Dosage and Administration: Adults. The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antipyretic or antipruritic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: Manifestations. Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are not effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

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50mg. Tablets **Talwin®**
brand of
pentazocine
(as hydrochloride)
in moderate to severe pain

Study of Cancer Origins Continues



Two lung sections, from a smoker, r., and a nonsmoker, are compared by Dr. Oscar Auerbach, Professor at New York Medical College. With the aid of an American Cancer Society grant, he plans a new study on the effects of smoking on the tracheobronchial tree and to continue investigations into origins of colon-rectum cancer.

Autotransplantation, Repair Promising in Kidney Lesions

Medical Tribune Report

PORTLAND, ORE.—Homologous kidney transplants may become less necessary in cases of renal artery lesions, and perhaps other kidney lesions, if preliminary work by a group of University of Oregon investigators on autotransplantation accompanied by microvascular repair stands the test of further experience.

Dr. Russell K. Lawson, Associate Professor of Urology, has reported two renal artery lesion cases for which nephrectomy was performed, the damaged kidney cooled and perfused, vascular repair performed with the aid of magnifying instruments, and the repaired kidney returned to the patient.

Dr. Lawson acknowledged that the autotransplantation and repair procedure is "really an extension of the technical aspects of transplantation." Since these "have pretty well been solved for most organ systems, particularly the kidney," he said, "it seemed a logical extension to use this technique now in other ways."

He noted that the technique could be used for other lesions of the kidney—for example, "in certain instances of difficult stone cases" or in "a solitary kidney with a tumor, where the surgeon can't be sure where the tumor starts and stops."

Dr. Lawson also observed that, while he knows of no attempts being made as yet to apply the autotransplantation-repair concept to other organs, "it certainly could be done with the liver or the heart."

External Repair Advantageous

External repair of the kidney, he said, has the advantages of ready accessibility of the renal artery and its branches for repair with small instruments, fine suture using 7-0 vascular silk and optical aids, as well as a long ischemic time in which to perform slow, meticulous repair of the artery without damage to renal function.

Perfusion, in a slush bath of Ringer's lactate solution containing heparin and procaine, Dr. Lawson remarked, gives "from five to eight hours of time to work on the kidney."

Of his two patients, Dr. Lawson stated, one was a 21-year-old woman with a five-year history of severe hypertension who was found to have stenosis of the right renal artery, with the kidney supplied entirely by collateral circulation.

At surgery, the right renal artery "was seen to be occluded by fibromuscular disease from its origin at the aorta to its bifurcation." Upon removal of the kidney, the diseased section of the artery was resected, leaving "just the branches going down deep into the kidney." By taking time and using the microvascular technique, Dr. Lawson said, a portion of the hypogastric artery with its branches was sutured onto the fine branches of the renal artery and the kidney then returned to the patient through standard transplantation techniques.

The other patient was a 31-year-old man with a congenital solitary left kidney who suffered an episode of gross hematuria three weeks before admission and

who was found to have an aneurysm involving the trifurcation of the renal artery.

With the kidney out of the body, the aneurysm was resected, leaving a small portion of the aneurysm wall containing the orifices of the main branches of the renal artery, to which a segment of the normal distal renal artery was anastomosed.

In this patient, the repaired kidney did not perfuse well, necessitating re-exploration and reimplantation from the flank to the right groin. And although "excellent revascularization" was then obtained, a prolonged period of acute tubular necrosis and poor renal function followed, requiring a cadaver transplant.

"The particular lesions that were present in these two cases," Dr. Lawson commented, "were not amenable to the usual kinds of surgery—that is, they required very delicate repair, and it would not have been possible to do it with the kidney in the body."

Without repair, he noted, in the case of the woman with renal artery stenosis, "we couldn't have done anything—the kidney would have had to have been removed." Operating on the kidney with the aneurysm, he said, "would have been a much riskier operation to perform, doing it in the usual way."

Coauthors were Drs. Clarence V. Hodges and Thomas M. Pitre.

TB Association Focused In 1971-72 on Shortages Of Facilities, Manpower

Medical Tribune Report

NEW YORK—Shortages of diagnostic and treatment facilities and of trained manpower received special attention from the National Tuberculosis and Respiratory Disease Association during 1971-72, the association said in its annual report.

Establishment of a nationwide consultation program offering hospitals on-site evaluation of respiratory disease facilities by a team of experts from another area was cited as a major effort to improve facilities.

Another national consultation service, for hospital administrators, was set up to facilitate treatment of tuberculosis patients in general hospitals. The NTRDA also joined with the American Hospital Association in drafting standards for general hospital treatment of TB.

Working with hospital accrediting authorities, the NTRDA developed standards for providing inhalation therapy in the hospital setting.

Efforts to increase the pool of trained manpower to treat emphysema and other respiratory diseases included the awarding of 24 fellowships, totaling \$196,464, by NTRDA to physicians and medical school faculty members in 1971-72. An additional 240 training grants and fellowships for both practicing physicians and medical students were awarded by state and local Christmas Seal associations.

Ultrasound Spots Unsuspected Pericarditis

Medical Tribune Report
LOS ANGELES—Clinically unsuspected heart disease has been detected in a high percentage of patients with rheumatoid arthritis by means of ultrasonic echocardiography, it was reported here by Dr. Paul A. Bacon, of the University of California at Los Angeles School of Medicine.

An echocardiography study of 22 patients with chronic rheumatoid arthritis who had subcutaneous nodules revealed the presence of a pericardial effusion in 50 per cent. Among a similar group with no detectable nodules, 18 per cent had an effusion.

No Effusions in Controls

In sharp contrast, no effusions were found in a control group of osteoarthritic patients who were matched for age and sex.

Dr. Bacon emphasized that none of the rheumatoid arthritis patients had shown symptoms of pericarditis at the time of the examination, and none had evidence of constriction. Only one patient had previously experienced the pain typical of pericarditis and in only one patient did an

electrocardiogram provide evidence of pericarditis.

The incidence of the disease seen in this series of patients is considerably higher than that noted by other investigators after careful and repeated clinical examinations, Dr. Bacon said. Since the over-all incidence of 34 per cent is very close to the accepted postmortem incidence of 30 per cent, he believes that the technique of echocardiography can give a "true estimate" of the prevalence of pericardial effusion in patients with rheumatoid arthritis.

Journals of the A.M.A. Will Employ Only Metric Units of Measurement

Medical Tribune Report

CHICAGO—Doctor, forget about inches, feet, and yards. Eschew the ounce and pound, as well as the pint and quart. Go metric!

That is what the American Medical Association is doing. J.A.M.A. and A.M.A.'s 10 specialty journals have banished the English system and will use only metric units of measurement henceforth.

As part of the same study, the rate of mitral valve movement was assessed in all three groups of patients. The mean rate observed in the rheumatoid arthritis patients with nodules proved to be significantly lower than the mean rate observed in the nonnodular group and far lower than that registered for the controls. A diminished rate of valve movement also showed a correlation with the duration and severity of the rheumatoid disease. Coauthor of the report was Dr. Derek G. Gibson, of St. Bartholomew's Hospital, London.

SURGICAL NOTES

Popliteal Artery Injury

LAS VEGAS, NEV.—In the dislocated knee with associated popliteal artery injury, arterial repair must be carried out within eight hours of injury if limb survival is to be assured, Drs. Neil E. Green and Ben L. Allen, Jr., of Duke University Medical Center, reported.

With arterial repair performed within that period, 87 per cent of limbs can be saved, they told the 40th annual meeting of the American Academy of Orthopaedic Surgeons.

When arterial repair is undertaken later, however, the limb salvage rate is about 12 per cent.

Emphasizing that the eight-hour time limit should never be exceeded, they said that "a maximum of six hours is actually a safer limit."

While arteriography gives little additional information, they said, it may be performed if the time interval between the injury and the completion of the surgical anastomosis is not delayed beyond the critical period.

Prophylactic fasciotomy is usually indicated at the time of arterial repair, the report noted, because of the marked increase in swelling after restoration of the circulation.

Surgery in the Elderly

LUBLIN, POLAND—Of some 3,000 patients who underwent vascular surgery over the past six years at a leading Milan, Italy, clinic, one in three was over 60. Of 857 who received surgical reconstruction using bypass with thromboectomy, one in five had passed the age of 70.

The prognosis in such interventions in elderly patients is now much more favorable, according to Dr. Edmondo Mada Professor of Surgery at the University of Milan.

Of patients receiving only conservative treatment in spite of indications for surgery, 70 per cent died within the first year, he said.

On the other hand, 58 per cent of those operated on survived for five years and 30 per cent for 10 years. The rate of amputations dropped from 20 per cent to 7.7 per cent in the 20-year period, Dr. Mada said in a review presented to the Society of Polish Surgeons.

He predicted that the indications for vascular surgery will broaden considerably.

"From my own observations, a conservative treatment was given to 76.4 per cent of patients 20 years ago," he said, "while it is only 47.5 per cent of our patients who undergo a conservative treatment now."

Skull Defects Treated

STOCKHOLM—Ribs are being transplanted by Swedish surgeons to amellate cranial defects.

Of 55 patients with skull defects due to trauma or neurosurgical intervention, 46 received rib transplants and nine received iliac transplants. Transplants were made under the skull on the dura, between bone edges under tension, and as "onlay" transplants, with several pieces of bone filling in the defect, Dr. Bengt Korlof, of Karolinska Hospital, reported.

One patient suffered a partial loss of transplant because of osteitis three years later, he told the annual meeting of the Swedish Medical Society. Good healing was seen in all other patients. Palpation showed a good closure of the defects, but in x-rays the contours of the individual transplant pieces were visible.

Dr. Korlof said that 50 per cent of cases showed a normal contour, 25 per cent a mild unevenness, and 25 per cent a more pronounced irregularity in contour. He recommended filling larger defects with pieces of rib and filling the smaller ones with bone material taken from the crista illiaca.

Wednesday, February 21, 1973

Hypnosis Held Anesthetic Base Of Acupuncture

Medical Tribune World Service

LONDON—Acupuncture's effectiveness as an anesthetic is due to hypnosis, asserts Dr. Patrick D. Wall, Professor of Anatomy, University of London, and co-developer of the widely accepted "gate control" theory of pain. Dr. Wall's assertion directly contradicts views of other physicians, who have sought to explain acupuncture's anesthetic effect by the selective activation of fibers to close a "gate" and prevent transmission of pain impulses to the brain.

It is unlikely that acupuncture stimulation generates pain-inhibiting impulses, since the "bizarreness" of the location of the needle insertion points corresponds to no "known pattern of nervous or other interactions so far discovered," Dr. Wall wrote in *New Scientist*.

The "key" factor suggesting that the anesthetic effect produced by acupuncture is due to hypnosis is that "the procedure is not used on children" in China despite the fact that there is "every reason to believe that all major mechanisms within a child's brain are functioning, certainly by the age of five," Dr. Wall said. "Hypnosis is a state in which the subject has handed over to the hypnotist all decisions about what type of behaviour is relevant. Reactions to tissue damage and pain are forms of behaviour, and these also can be controlled under conditions of deep hypnosis. Children, who are highly suggestible in some ways, are not open to the sophisticated transfer of responsibility which is required for hypnosis. Children are not placebo reactors. In the West, they have not had time to learn our general belief that the syringe needle transmits relief of suffering. In China, it appears that children have not had time to learn that the acupuncture needle has the same magical properties."

Patients Choose Procedure

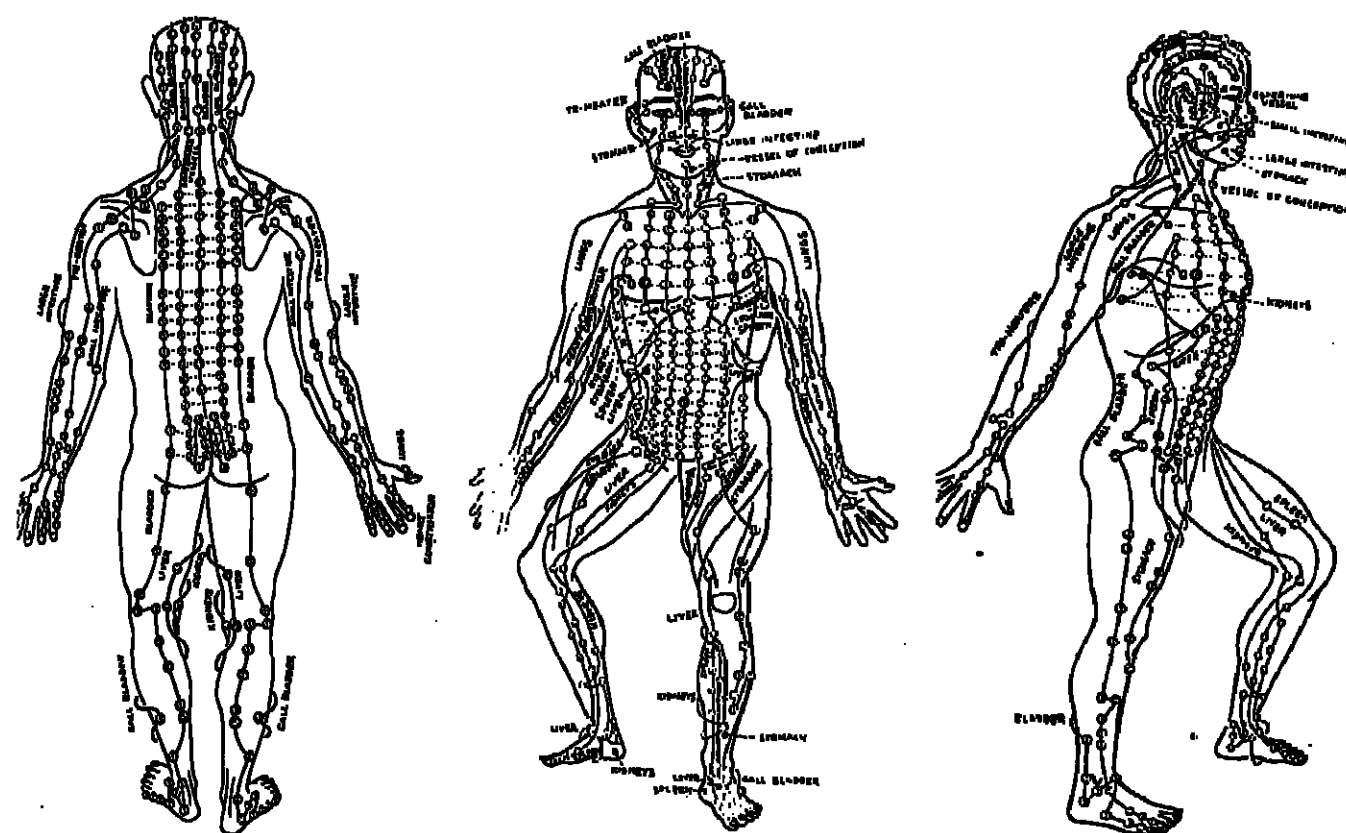
"Most important," continued Dr. Wall, "we are told [by the Chinese] that the patients themselves choose whether they will have acupuncture or general anaesthesia. They are given prolonged instruction extending over days," which reinforces traditional beliefs regarding acupuncture as a "powerful medicine."

The report that "some Chinese patients fail to respond to acupuncture anaesthesia is further evidence that we are dealing here with a highly personal therapy such as hypnosis, rather than an effect of some system common to all mankind, such as [that produced by] the action of ether...."

The modern technique of running electricity through the acupuncture needles "would serve to maintain the patient's attention and inform him that something was being done to him," stated Dr. Wall.

However, attributing acupuncture's anesthetic effect to hypnosis "in no way dismisses or diminishes the value of acupuncture, but it does place it in a class of phenomena with which we are partly familiar," observed Dr. Wall, adding that acupuncture may be superior to drug anaesthetics "in that it would leave the homeostatic mechanisms of the body intact and undrugged."

Dr. Wall concluded that "acupuncture anaesthesia presents a fascinating challenge to the 'objectivity' of Western science and its application to man. It challenges cultural, scientific and political biases. We must face the fact that it exists, and test the question of whether, when it works, it is better for the patient than general anaesthesia." And, if it is a type of hypnosis, Dr. Wall said, then "should we now teach school children that no pain will be felt in an operating theatre or during childbirth when the expert carries out the appropriate manipulation?"



Illustrations from Chinese Acupuncture show meridian and acupuncture points.

Book Gives Diagrams of Acupuncture Points

Medical Tribune Report

NEW YORK—Shown above are diagrams depicting acupuncture points and meridians, taken from *Chinese Acupuncture*, by Dr. Wu Wei-Ping, president of the Chinese Acupuncture Society and head of the School of Acupuncture in Taipei. The newly translated book, published initially in France, is one of the first in English to present detailed diagrams of acupuncture points, with accompanying explanations of point-by-point treatment. The British Book Center, New York, is the U.S. distributor of the book.

Acupuncture theory holds that particular points of the skin are indicators of the state of health of certain organs and their functions. These points do not appear randomly but occur in lines, or meridians. Twelve regular (i.e., having bilateral symmetric branches) and two "special"

(not associated with any organ, but nonetheless also serving as a channel for the flow of "energy") meridians are shown above. Though there are more than 12 organs in the body, the other parts are considered under the regulation of one or more of these 12 organ systems.

Treatment Varies With Time

Trained acupuncturists treat more than one meridian simultaneously. Treatment also varies according to the time of day, season, condition of the patient, and the disorder.

Acupuncture points are located, according to Dr. Wei-Ping, by *pouce* and *fen*. The term *pouce* refers to an anatomic unit of measurement that varies according to both the individual and the body part concerned. For example, the *pouce* for the arm is defined as "the 9th part of the

distance between the crease of the axilla and the crease of the elbow." A *fen* is a "decimal" part of the *pouce*, Dr. Wei-Ping says. A typical description, taken from the book, follows: point number 1 (on the 11-point lung meridian) is called Chung Fu. It is "located two *pouces* lateral to the nipple and four *pouces* eight *fen* above it, in the first intercostal space." Needling instructions are: "3.5 *fen* deep." Indications include "dyspnoea, bronchitis, tonsillitis, tropical fevers, pulmonary affections, cardiac affections, oedema of the face or limbs."

Moxibustion is used by many classical Asian acupuncturists for certain disorders, says Dr. Wei-Ping. It consists of the burning of a small cone—about the size of a rice grain—of dried *Artemisia* leaves over certain of the acupuncture points. Its use is specifically forbidden in some cases.

'Gate Control' Theory of Pain Is Explained

MEDICAL TRIBUNE recently interviewed Ronald Melzack, Ph.D., who with Dr. Patrick D. Wall evolved the "gate control" theory of pain, which is the most widely cited concept in Western discussions of the reported effectiveness of acupuncture. Dr. Wall's views of acupuncture are reported elsewhere on this page. The report of the interview with Dr. Melzack follows.

The modern technique of running electricity through the acupuncture needles "would serve to maintain the patient's attention and inform him that something was being done to him," stated Dr. Wall. However, attributing acupuncture's anesthetic effect to hypnosis "in no way dismisses or diminishes the value of acupuncture, but it does place it in a class of phenomena with which we are partly familiar," observed Dr. Wall, adding that acupuncture may be superior to drug anaesthetics "in that it would leave the homeostatic mechanisms of the body intact and undrugged."

Dr. Wall concluded that "acupuncture anaesthesia presents a fascinating challenge to the 'objectivity' of Western science and its application to man. It challenges cultural, scientific and political biases. We must face the fact that it exists, and test the question of whether, when it works, it is better for the patient than general anaesthesia."

And, if it is a type of hypnosis, Dr. Wall said, then "should we now teach school children that no pain will be felt in an operating theatre or during childbirth when the expert carries out the appropriate manipulation?"

He cited as examples that the intensity of pain is not proportional to the extent of the injury; the quality of pain is determined by previous experience and how well we remember it. Pain is also influenced by its significance in the individual's culture, and it has a strong emotional character in addition to its sensory properties.

Central to the gate control theory of pain mechanisms is the substantia gelatinosa throughout the length of the spinal cord. He and Dr. Wall hypothesized that this area acts as a gate control system modulating the transmission of nerve impulses. They suggest that the large myelinated fibers inhibit pain signals, while the small myelinated fibers facilitate their transmission. In each case, this is accomplished by the action of the substantia gelatinosa on spinal cord cells that transmit afferent signals to the brain.

Offers Refinement of Theory

In a refinement of the theory, Dr. Melzack has put forward the view that a portion of the brain-stem reticular formation acts as a "central biasing mechanism" by exerting a tonic inhibitory influence (or bias) on information transmission at all synaptic levels of somatic projection.

The theory proposes that pain signals may produce a long-lasting change in the central nervous system itself, which is maintained or triggered by somatic and sympathetic inputs and by brain activities.

"To take the case of phantom limb pain, it cannot be explained," Dr. Melzack pointed out, "by any single mechanism, such as peripheral nerve irritation, sympathetic inputs, or psychopathology. All contribute in some way. The question is How?"

"Investigators have sought mechanisms in the spinal cord itself. That pathway has been cut at every level up to the brain—often without significant pain relief. That is not to say that spinal transmission has

no role, but it must be a part of a more pervasive system."

The gate control theory suggests the answer, and its main therapeutic outcome would be that pain signals can be inhibited or blocked by neurophysiologic events. Further, the "gate" can be closed by brain activities.

But it is in the psychologic sphere that research is now going on at Montreal's Lethbridge Rehabilitation Center. There Dr. Melzack, with Dr. Serge Blakodoff, medical director, has started investigative work in two areas—back pain and pain following amputation.

"In these states," Dr. Blakodoff told MEDICAL TRIBUNE, "Dr. Melzack will seek forms of treatment in which the gate control theory can apply. Particularly, he will interest himself in the residual group of pain problems that does not respond to current therapies—whether somatic or psychic."

"The gate control theory hypothesizes that the experience of pain can be intensified or decreased by psychological factors. As shown in biofeedback experiments, brain control over sensory input is reflected in alpha EEG waves. Using such techniques as relaxation, strong suggestion, and hypnosis, patients will be taught to control their own EEG activity."

"In the case of chronic back strain, for example, where there has been an irreversible pain cycle, the patient will learn to concentrate in such a way as to reduce pain perception. A tone tells the patient when he is producing alpha waves."

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INDICATIONS: Primarily for severe or sustained elevation of blood pressure (particularly diastolic) and almost all forms of fixed and progressive hypertensive disease, even when blood pressure elevation is moderate. Not recommended for labile or mild forms of hypertension.
CONTRAINDICATIONS: Proven or suspected pheochromocytoma; hypersensitivity to Ismelin. Do not use with MAO inhibitors.
WARNINGS: Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Warn patients not to deviate from instructions and about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking Ismelin.
Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.
If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer proanesthetic and anesthetic agents cautiously in reduced dosage with oxygen, atropine, and vasopressors ready for immediate use. Give vasopressors with extreme caution because patients on Ismelin may have a greater propensity for cardiac arrhythmias.
Fetile illness may reduce dosage requirements. In frank congestive heart failure not due to hypertension, Ismelin is not recommended. Due to catecholamine depletion and increased responsiveness to myocardial infarction, special care is required when treating patients with a history of bronchial asthma, since the condition may be aggravated.
Use in Pregnancy: The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

PRECAUTIONS: Give very cautiously to hypertensives with (a) renal disease with nitrogen retention; (b) coronary disease with insufficiency or recent myocardial infarction; (c) cerebral vascular disease, especially with encephalopathy; and (d) no severe congestive failure. Watch for weight gain or edema in patients with congestive cardiac decompensation. If digitalis is used with Ismelin, remember that both drugs slow the heart rate.
Arythmogenic drugs (e.g., amphetamines), mild stimulants (e.g., sympathomimetics), and triethylamine derivatives (e.g., triethylamine, triethylamine) may decrease the hypotensive effect of Ismelin. Wait one week after discontinuing MAO inhibitors before starting Ismelin.
Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts, and liver function tests are advised during prolonged therapy.

ADVERSE REACTIONS: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. Less frequently—dyspepsia, fatigue, nausea, vomiting, recturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (anginal), chest parasthesia, nasal congestion, weight gain, and asthma in susceptible individuals.

DOSE AND ADMINISTRATION: Initial dosage should be low and increased gradually by small increments.

HOW SUPPLIED: Tablets, 10 mg (pale yellow, scored) and 25 mg (white, scored); bottles of 100 and 1000.

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Clinical Trials



FDA Proposes Standards of Quality For Bottled Drinking Water on Sale

BETHESDA, MD.—The Food and Drug Administration has proposed standards of quality for bottled drinking water sold for human use. They would be the U.S. Public Health Service Drinking Water Standards (1962) with modifications of the sampling methods and bacteriologic limits. These are the same standards for water used by interstate common carriers and are the basis for state and local regulation of public drinking water supplies. The proposal establishes bacteriologic, physical, chemical, and radioactivity limits and sets forth the sampling method.

The American Bottled Water Association, which represents producers of 96 per cent of bottled water sold in the United States, recently reported annual sales in excess of \$100,000,000, far above what they were a few years ago. Analyses have shown, the FDA said, that some bottled water fails to meet the current standards for drinking waters.

Keeping the mild hypertensive in his place

Still unsurpassed as a basic diuretic-antihypertensive, Esidrix has the gradual onset and sustained blood-pressure lowering effect needed in the long-term management of mild hypertension. We call it antihypertensacy.

And as a diuretic, Esidrix is useful in many forms of edema.

Contraindications include anuria. Use with caution in patients with impaired renal or hepatic function.



Esidrix[®] (hydrochlorothiazide)
Indications: Hypertension and edema. Contraindications: Anuria, hypersensitivity to thiazides or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous. Warnings: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma. Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potential adverse effects include hypotension or peripheral edema. A history of allergy or bronchial asthma. The possibility of exacerbation or activation of reported lupus erythematosus has been reported.

Usage in Pregnancy: Use of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers: Thiazides cross the placental barrier and appear in cord blood and breast milk. Precautions: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is receiving excessive or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular rigidity, oliguria, tachycardia, and gastrointestinal disturbances such as nausea or vomiting. Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH. Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exacerbate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice. Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy. Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration. Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use. If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy. Thiazides may decrease serum PBI levels without signs of thyroid disturbance. Adverse Reactions: Gastrointestinal—nausea, gastric irritation, anorexia, vomiting, cramping, diarrhea, constipation, jaundice (irreversible cholestasis), pancreatitis, Central Nervous System—dizziness, vertigo, paresthesias, headache, xanthopsia. Dermatologic—Hypersensitivity—purpura, photosensitivity, rash, urticaria, necrotizing angitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. Hematologic—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. Cardiovascular—Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Other—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever severe reactions are moderate or severe, reduce dosage or withdraw therapy. Dosage: Individualize dosage by titrating for maximum therapeutic response at the lowest possible dose. Hypernatremia—Initial—Usual dose 75 mg daily. Maintenance—After a week dosage may be adjusted downward to as little as 25 mg or upward to as much as 100 mg daily. Combined therapy—When necessary, other antihypertensive may be added gradually and with caution because of the potentiating effect of this drug. Dosages of ganglionic blockers should be halved. Edema—Initial—25 to 200 mg daily for several days. Maintenance—25 to 100 mg daily or intermittently. Refractory patients may require Supplied: Tablets, 50 mg (yellow, scored) and 25 mg (pink, scored) bottles of 100, 1000, and 5000.

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Immunity Against Tumor

BUFFALO, N.Y.—J. George Bekesi, Ph.D., of Roswell Park Memorial Institute here, has reported experimental success with stimulation of immunity against tumor by neuraminidase-treated tumor cells.

Dr. Gerald P. Murphy, institute director, commented that Dr. Bekesi's work "lays the foundation so that we can safely introduce the neuraminidase approach at the human level."

Dr. Bekesi said that neuraminidase releases some 65 to 70 per cent of the malignant cells' surface sialic acid. The removal of this complex carbohydrate moiety from the terminal position of the surface glycoprotein allows the tumor cells to express their antigenicity. Then, using the neuraminidase-treated leukemic cells as an immunogen, one can elicit specific immunologic response to the tumor, Dr. Bekesi said.

"Thus treated," he continued, "leukemic cells cannot initiate new tumor growth; mice injected with 10,000,000 neuraminidase-treated cells did not develop leukemia. But mice repeatedly immunized were refractory to a challenge of 5,000,000 viable leukemic cells, while the control animals died after receiving only one cell."

Psychotherapeutics

ROCKVILLE, MD.—A computerized information system developed by the National Institute of Mental Health to facilitate research on psychotherapeutic drugs will be tested for speeding the Food and Drug Administration's review of proposed new drugs for safety and efficacy before they are placed on the market. The cooperative project is scheduled for completion in one year.

The computerized system, called the Research Plan Report, was developed by the Psychopharmacology Research Branch of NIMH. It is said to provide an efficient means for storing and retrieving the highly technical data generated by the branch's grant-supported program.

Lung Disease Research

BOSTON.—A five-year investigation into pulmonary and cardiovascular diseases has been launched by the Harvard Medical School with a grant from eight tobacco companies and an association of tobacco growers.

The study will be conducted in the Harvard Medical Unit and the Channing Laboratory of the Boston City Hospital with Dr. Gary L. Huber, Assistant Professor of Medicine, as the principal investigator.

"At this time, we already have an extensive research program concerned with the effects of environmental influences on the lung," Dr. Huber said. "Among a variety of other environmental influences to be studied, attention will now also be given to any specific effects cigarette smoke may have in the development of such pulmonary diseases as emphysema, chronic bronchitis, and lung cancer, and heart and vascular diseases."

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for psychic tension...



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And should you choose to prescribe Valium, you should also keep this information in mind. It is usually well tolerated; side effects most commonly reported have been drowsiness, fatigue and ataxia. Patients taking Valium should be cautioned against operating dangerous machinery or driving.

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Dependable response

The psychotherapeutic effect of Valium (diazepam), characterized by symptomatic relief of tension and anxiety, is generally reliable and predictable.

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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or

Prompt action

Significant improvement usually becomes apparent during the first few days of Valium therapy. Some patients may, however, require more time to establish a clear-cut response.

severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in

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salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. **Adults:** Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially; increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

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One Man... and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune



Prisoners, Patients, and 'Guinea Pigs'

FOR YEARS we've seen the relationship between prisons, medicine, and research as a shifting and unhappy set of interchanges. Tom Wicker, of the *New York Times*, has ranged the field. He has addressed the problem of Attica and the planned programs of Dr. Martin Groder, psychiatrist in the Federal Bureau of Prisons. He has discussed the application of electroshock, psychosurgery, and massive drug-

Wicker says, "Prison-run behavior research is in bad odor." I can understand this. In fact, I wonder how much of prison research is, in a medical sense, soundly based. My reasons would not be known to most investigators. I recall, many years ago, early investigations of antibiotics on prison populations. At that time, on the basis of our own clinical and experimental observations, I felt that the findings on patients in mental hospitals could not be extrapolated to general populations and, in fact, could be misleading.

Physiologic Differences

During my group's studies of hospitalized psychotic populations, we had found that schizophrenics would have an enormous tolerance to such substances as histamine, thyroid, sex steroids, etc. This high tolerance has not been generally reported or recognized. We had also observed a very low incidence of allergies, peptic ulcer, and ulcerative colitis during the active psychotic process. As has been confirmed elsewhere, we found a much lower incidence of malignancy in the schizophrenic population. It appeared to us that one might not be able to properly appraise the incidence of drug side effects in a prison population as typical of the general population, for it could be heavily skewed by a high incidence of schizophrenia. Interestingly, the high freedom from side effects found for the antibiotic under study then was later shown to be atypical for patients in practice. Our concern with the use of prison populations as experimental subjects was thus in a sense physiologically based. In respect to the use of irreversible procedures, such as psychosurgery and even the more benign electroconvulsive shock (ECT), one could only say that we were, and remain, violently opposed to the former in patients as well as prisoners. We would be reluctant to accept ECT as a prison procedure except under the most meticulous diagnostic work-ups and only under such absolute indications as severe, unresponsive involutional depression.

True Drawbacks

With increasing frequency questions are being raised as to the ethics involved in the utilization of prisoners as participants in controlled, experimental studies. That there is cause for concern, let no one doubt. But, here as in so much of what we confront these days, we must discriminate between what is abuse and what is valid. To deny a prisoner the right to volunteer as a participant in clinical experimentation may also be viewed as a denial of a civil and humane right that can be exercised by nonprisoners. To infer that all experiments carried on in prisons are done under direct or indirect coercion is to exclude a valid and perhaps even rehabilitative measure even as it denies the civil right of participation. We nonetheless find that the use of prisoners for clinical research confronts us with two drawbacks:

1. The fact that the investigation is being carried out on an atypical population and may not be projectable to non-prison populations.
2. It is carried out under the cloud of implied coercion.

What is the Real Opportunity?

This brings us to a very realistic opportunity with both social and medical poten-

tials. Prison populations should be carefully screened psychiatrically. Prisoners with manifestations of mental and emotional disorders should be diagnosed and kept in separate institutions, suitably equipped and staffed. At present this is only done in such situations as murder when insanity has been pled and the individual is committed to an institution for the criminally insane. The more general separation of criminals on a psychiatric basis would enable a more realistic approach to rehabilitation, with psychiatrically ill patients receiving suitable therapy and nonpsychiatric patients neither exposed to the mentally ill nor the administration of psychoactive drugs or procedures. This would make possible a more scientific approach in the event these two separate populations were to be considered for participation in clinical pharmacologic research.

I sometimes wonder whether those who out of hand condemn clinical investigations in prisons fully realize the implications of their position. Usually these are the same people who object to research in the institutions for the mentally retarded. Let us now also consider the rights of other children and minors. Do parents have the right to expose a child to such investigations as took place for polio vaccine? Let us consider the rights of the elderly. Are they completely qualified to decide on their participation, to give informed consent? Let us consider the rights of those who are feeble and those who are sick. Are they in a position to either risk or to participate in clinical-pharmacologic experimentation? No, this is not a *reductio ad absurdum*. The clinical participation of many of these groups has already been challenged, and, in respect to the young, the Commissioner of the FDA, Dr. Charles C. Edwards, has already pointed to a therapeutic wasteland—today as much as 50 per cent of new drugs have no recognized or proven dosage range for children.

Our Interdependence

We will yield to none in our desire to protect the rights of individuals, be they in or out of prison, the young or the old, the sick or the well. But if we are to protect our people against disease, diminish disability, and defer death, we must face the obligation and the recognition that neither prisoners nor others are "guinea pigs," but all of us are interdependent; that all must have the opportunity, if not the obligation, to participate in the discovery and definition of procedures for the protection of health and prolongation of life; and that we can and should have the most precise and effective safeguards that are realistically possible. Without eight-year-old James Phipps, whom Jenner inoculated, we still might have smallpox epidemics. Without Joseph Meister and Jean Baptiste Jupille, whom Pasteur treated for rabies, we might still be without antirabies vaccine. And without the risk in which thousands or tens of thousands of children took part, we would still have polio epidemics. We must demand and accept the good faith of all concerned with human experimentation. We ask those who object to human experimentation and clinical pharmacology to act in good faith and propose how science can discharge its obligations to them, to their families, and to their fellow men.

Corticosteroid Use in Shock Subject of Divergent Views

Continued from page 1

ditionally received early therapy with methylprednisolone succinate (in doses of 30 mg./Kg.), 70 per cent survived.

A similarly high salvage rate was also reported by the Minnesota investigator among a small number of patients with traumatic shock treated early with a corticosteroid.

Other data to support his contention that steroids can play a significant role in shock therapy included a survival rate of about 70 per cent in patients given a corticosteroid very early in the treatment of myocardial infarction and one of over 80 per cent in patients who had undergone cardiac surgery.

"The corticosteroids methylprednisolone succinate, hydrocortisone phosphate, and dexamethasone phosphate have generally increased survival," Dr. Lillehei said. "And we can usually correlate that survival with an improvement in the hemodynamic and metabolic picture—a shift back toward normal of all the changes that characterize stagnant anoxia."

Treatment Plan Comprehensive

Dr. Lillehei emphasized that the overall plan of treatment used at his center is necessarily comprehensive. Depending on specific indications, action is taken to control and correct blood loss, eliminate the sources of septic focus, and treat such manifestations as oliguria or hypoxemia. Many agents other than corticosteroids may be administered, he said.

The investigator also emphasized that the studies he cited had not been controlled. Although he believes that controlled studies "will have to be done," he said the task would be difficult because physicians who have observed the effects of corticosteroids in shock "won't allow their patients not to be treated."

But to fellow panelist Dr. Donald Kaye, of the Medical College of Pennsylvania, the lack of controlled studies is a major bar to acceptance of evidence now being reported from clinical trials.

"My plea is for controlled double-blind studies," he declared. "You cannot evaluate retrospectively; you cannot evaluate in a non-double-blind way. It just does not work."

Dr. Kaye noted that investigators have been coming out strongly since the mid-1960s in favor of large doses of steroids as treatment of shock. In this period, numerous controlled studies "should have and could have" been done, since the total number of patients was adequate to have proved or disproved the efficacy of the drugs.

"If I got up in front of physiologists and pharmacologists and presented a noncontrolled, nonblind, sequential type of study that showed a survival rate of, say, 60 per cent versus 20 per cent, it would be very unconvincing to them—they would not accept it because they would ask for controls," Dr. Kaye commented.

"I'm not saying that clinical evaluations are not provocative and do not provide evidence that we need to go ahead and get good controlled studies," he went on. "What I am saying is that there is no substitute for such good controlled studies and I cannot be convinced on the basis of what really is a testimonial."

Multicenter studies will be advisable, Dr. Kaye suggested, to make sure that different types of patient are included and to balance different inherent biases.

During a subsequent exchange of views, Dr. Lillehei backed the idea of a university group study, but asked symposium participants to remember that many therapeutic agents—including a "good

share of the antibiotics"—are now in widespread use "without ever having been subjected to a double-blind study."

"In the meantime," he said, "I think that those who don't actively plan to do a study themselves would best err on the side of using this therapy because I believe the evidence is very strong to support it."

Arguments for taking a middle-of-the-road course were put forward by Dr. Max Harry Weil, of the University of Southern California School of Medicine, who said he hoped that clinicians would leave the symposium with a nonpolarized point of view—seeing the use of corticosteroids for selected types of shock as "not necessarily either an obligation or malpractice."

In Dr. Weil's opinion, there is now substantial experimental data to indicate that glucocorticoids have hemodynamic, cellular, and perhaps biochemical enzymatic actions that protect laboratory animals under conditions of a reduction in perfusion and blood flow and that these effects apparently lead to increased survival.

Reports of the drugs' use in patients have shown some parallel physiologic and biochemical changes, he said, adding that such parallels provide ample incentive "to look very seriously at circumstantial evidence" that favors the use of corticosteroids in a clinical environment.

Dr. Weil agreed that clinical studies so far have generally consisted of uncontrolled experimentation with retrospective analysis of results. He believes the need for controlled studies has become obvious, and he commented that he looks for them to be made in cities like Boston, New York, and Baltimore, "where there is a lack of prejudice for the use of these agents."

Nevertheless, this investigator considers it erroneous to take the "extreme" stand that patients must be studied as objectively as animals or that lengthy controlled studies must invariably take place before a therapeutic agent is accepted. (Like Dr. Lillehei, he pointed out that little time had been needed after the introduction of penicillin to recognize its effectiveness.)

Specializes in Bacterial Shock

Referring to studies of bacterial shock—an area in which he has specialized—Dr. Weil noted that clinicians would find it difficult at the bedside to assign patients to a treatment or nontreatment group in the same randomized fashion employed in the laboratory. Also, under investigative protocols, they would have to inform patients of the assignments.

A further problem, he said, is the fact that the numbers of patients who might be identified by relatively established criteria for bacterial shock are not generally sufficient to allow studies on a large population basis.

An evaluation of reports about specific types of shock has led Dr. Weil to conclude that the parallels between experimental and clinical models of bacterial shock warrant the early use of corticosteroids. He also thinks that "the evidence is mounting" for use of the agents in management of shock complicated by myocardial infarction.

In treating hypovolemic shock, he said, he would probably not employ corticosteroids "as a routine maneuver," but he believes their use could be considered in hypovolemia complicated by either bacteremia or myocardial failure.

But Dr. Weil would not adopt the concept of using the corticosteroids as a "general drug" in treatment of shock, regardless of cause.



DR. WEIL

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All cases of hypertension except the mildest and the most severe.

CONTRAINDICATIONS

Esimil
Guinea pig: Proven or suspected pheochromocytoma; hypersensitivity to guanethidine. Do not use with MAO inhibitors.

Hydrochlorothiazide: Anuria; discontinuous drug if renal shutdown occurs for any reason. Progressive hepatic disease may accelerate development of hepatic coma. Do not give to patients with known allergy to thiazides or other sulfonamide-derived drugs.

Ser-Ap-Es

Reserpine: Known hypersensitivity; mental depression, especially with suicidal tendencies; active peptic ulcer; ulcerative colitis; digitalis intoxication; aortic insufficiency; electroconvulsive therapy.

Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease. **Hydrochlorothiazide**: See hydrochlorothiazide section above.

WARNINGS

Antihypertensives are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with all drugs and their combinations before prescribing, and patients should be warned not to deviate from instructions.

Esimil
Guinea pig: Warn patients about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during initial dosage adjustment and with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking guanethidine. Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazards of cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage with oxygen, atropine, and vasopressors ready for immediate use. Give vasopressors with extreme caution because patients on guanethidine may have a greater propensity for cardiac arrhythmias. Febrile illness may reduce dosage requirements. Due to catecholamine depletion and increased responsiveness to norepinephrine, special care is required when treating patients with a history of bronchial asthma, since the condition may be aggravated.

Hydrochlorothiazide: Small bowel stenosis, with or without ulceration, has been associated with use of enteric-coated thiazides with potassium, and with enteric-coated thiazides alone. These bowel lesions have caused obstruction, hemorrhage, and perforation; surgery was frequently required and deaths have occurred. Available information tends to implicate enteric-coated potassium salts. Therefore, coated potassium-containing formulations should be used only when dietary supplementation is not practical and discontinued immediately if abdominal pain, distention, nausea, vomiting, or GI bleeding occurs.

Lowering of blood pressure in hypertensive patients may sometimes result in nitrogen retention, and also result in reduced renal blood flow, particularly in those with impaired renal function. In progressive renal insufficiency, as observed, discontinuance of drug may be desirable with renal disease, thiazides may precipitate azotemia. Continued use may develop in those with impaired renal function. Pay special attention to electrolyte balance of patients with severe hepatic insufficiency, in whom hypokalemia and azotemia may develop. Watch for symptoms of impending hepatic coma (confusion, drowsiness, tremor) and last for increased arterial ammonia concentration, sodium and potassium excretion. Thiazides may decrease glucose tolerance; use cautiously in diabetics. Hyperuricemia may occur but is generally reversed by a uricosuric agent. Thiazides may decrease arterial responsiveness to norepinephrine and increase responsiveness to tubocurarine. If possible, withdraw therapy 2 weeks prior to surgery. Hypertensive episodes under anesthesia have been observed. If emergency surgery is indicated, preanesthetic and anesthetic agents should be administered in reduced dosage.

The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma.

Ser-Ap-Es

Reserpine: Discontinue at first sign of depression, since mental depression (which may be severe enough to result in suicide) can occur with reserpine and may persist for several weeks after drug withdrawal. Use with extreme caution in those with a history of depression.

Discontinue reserpine for 2 weeks before giving electroconvulsive therapy. MAO inhibitors should be avoided or used with extreme caution. **Hydralazine**: Hydralazine, particularly if given daily for prolonged periods in doses over 400 mg, may produce an arthritis-like syndrome leading to a clinical picture simulating acute systemic lupus erythematosus. In rare instances, this may occur at lower doses. Most of these reactions are reversible upon withdrawal of therapy, but long-term treatment with steroids may be necessary. An L. E. cell preparation is indicated in the presence of any unexplained symptoms.

Use MAO inhibitors with caution. **Hydrochlorothiazide**: See hydrochlorothiazide section above.

Use in Pregnancy

Esimil
Guinea pig: The safety of guanethidine for use in pregnancy has not been established; therefore, the drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

Hydrochlorothiazide: Thiazides should be used with caution in pregnant or lactating patients since this drug crosses the placental barrier and appears in breast milk and may result in fetal hyperbilirubinemia, thrombocytopenia, or altered carbohydrate metabolism. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

Ser-Ap-Es

Reserpine: The safety of rauwolfia preparations for use in pregnancy or lactation has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment

of the physician, its use is deemed essential to the welfare of the patient. Reserpine crosses the placental barrier and appears in breast milk. Therefore, increased respiratory tract secretions, nasal congestion, cyanosis, and anorexia may occur in infants born to mothers treated with the drug.

Hydralazine: Although there has been no adverse experience with hydralazine in pregnancy, the drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

Hydrochlorothiazide: See hydrochlorothiazide section above.

PRECAUTIONS

Esimil
Guinea pig: Give cautiously to patients with severe coronary insufficiency, recent myocardial infarction, or cerebrovascular insufficiency. Give Esimil with extreme caution to those with severe cardiac failure.

Appetite suppressants (eg, amphetamines), mild stimulants (eg, ephedrine, methylphenidate), and tricyclic antidepressants (eg, imipramine,

why Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

because only Ser-Ap-Es adds hydralazine to rauwolfia-thiazide



Ser-Ap-Es does more than control blood pressure in moderate hypertension—it's a therapeutic approach that considers the whole patient. And adding hydralazine to rauwolfia-thiazide

usually permits lower dosage of each component than if prescribed alone.

If there is slight renal impairment, hydralazine helps maintain or increase renal blood flow.

If the patient is stress reactive, the reserpine component should have a calming effect.

If the patient is uncooperative, Ser-Ap-Es may be a help because it contains all the medication many patients need in a single tablet.

Ser-Ap-Es should be used with caution in patients with advanced renal damage and cerebrovascular accidents. It should be discontinued at the first sign of mental depression.

why Esimil®

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

because Esimil offers the control-with-convenience so many hypertensives need



Esimil, an equally valuable yet different approach to moderate hypertension, makes sense for many patients because it anticipates future problems while helping to solve present ones.

If the patient is free of organ damage, Esimil may help keep her that way because it provides guanethidine, perhaps the most effective antihypertensive available. And effective lowering of blood pressure takes pressure off target organs.

If the patient forgets things, Esimil may make it easier to remember with once-a-day dosage, feasible in most cases.

Postural hypotension may occur with the use of Esimil, particularly while the drug is being introduced. Like all antihypertensives, Esimil should be given with caution in the presence of severe coronary insufficiency or recent myocardial infarction.

early, effective control of hypertension can save lives

propranolol, doxapram) may decrease the hypotensive effect of guanethidine. Wait one week after discontinuing MAO inhibitors before starting guanethidine.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver function tests are advised during prolonged therapy.

Hydrochlorothiazide: Perform serum potassium, BUN, uric acid, and blood sugar tests prior to and at appropriate intervals during therapy. Watch for clinical signs of fluid or electrolyte imbalance (hypopotassemia, hypochloremia, alkalosis, hypokalemia). Warning signs: dryness of mouth, thirst, weakness, or cramps, muscular fatigue, hypotension, lightheadedness, dizziness, muscle pains, or drowsiness. GI disturbance. Serum and urine electrolyte determinations are particularly important when patient is vomiting excessively, receiving parenteral fluids, or on ACTH or corticosteroids. In presence of severe hyponatremia, sodium restriction, or ACTH or corticosteroids.

Interference with adequate oral intake of electrolytes may also contribute to hypokalemia. Digitalis may exaggerate metabolic effects of hypokalemia especially with reference to

myocardial activity. (Signs of digitalis intoxication may be produced by formerly tolerated doses of digitalis.) Hypokalemia may be avoided or treated with supplemental potassium or potassium-rich foods. Supplemental potassium is indicated when serum potassium is 4 mEq/liter or less, or if patient is receiving digitalis. Chloride deficit may be corrected with ammonium chloride (except in those with hepatic or renal disease) and largely prevented by a nonacid salt intake. If dietary salt is unduly restricted, especially during hot weather, in severely edematous patients with congestive heart failure or renal disease, a low salt syndrome may complicate therapy with thiazides.

Transient elevations in plasma calcium may occur in patients taking thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia (or frank gout) may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide therapy.

If nitrogen retention indicates onset of renal impairment, discontinue drug.

Ser-Ap-Es
Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or other GI disorders. May precipitate biliary colic in patients with gallstones.

Take special care with asthmatics and in hypertensives with renal insufficiency. Use cautiously with digitalis, quinidine, and guanethidine. Intraoperative hypotension has occurred in hypertensive patients receiving rauwolfia preparations, but withdrawal of reserpine does not assure that circulatory instability will not occur in such patients.

Hydralazine: Use cautiously in suspected coronary artery or other cardiovascular disease, cerebrovascular accidents, and advanced renal disease. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyretic effect and addition of pyridoxine to the regimen if symptoms develop. Blood dyscrasias consisting of reduction in hemoglobin and red cell count, leukopenia,

agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.

ADVERSE REACTIONS

Esimil
Guinea pig: Frequent reactions due to sympathetic blockade—dizziness; weakness; lassitude; syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia; increase in bowel movements; diarrhea (which may be severe and require discontinuation of the drug). Other common reactions— inhibition of ejaculation; fluid retention; edema; congestive heart failure. Less frequent—drowsiness; nausea; vomiting; nocturia; urinary incontinence; dermatitis; scalp hair loss; dry mouth; rise in BUN; pools of the legs; blurring of vision; parotid tenderness; myalgia; muscle tremor; mental depression; chest pains (angina); chest paresthesias; nasal congestion; weight gain; and asthma in susceptible individuals.

Hydrochlorothiazide: Gastrointestinal—anorexia; gastric irritation; nausea; vomiting; cramping; diarrhea; constipation; jaundice (intrahepatic cholestasis); pancreatitis; hyperglycemia; glycosuria. Central Nervous System—dizziness; vertigo; paresthesias; headache; xanthopsia. Dermatologic—hypersensitivity—purpura; photosensitivity; rash; urticaria; necrotizing angitis; Stevens-Johnson syndrome; and other hypersensitivity reactions. Hematologic—leukopenia; thrombocytopenia; agranulocytosis; aplastic anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Muscular—muscle spasms; weakness; restlessness. When severe adverse reactions are moderate or severe, reduce dosage or withdraw the drug.

Ser-Ap-Es
Reserpine: Gastrointestinal—hypersecretion; nausea; vomiting; anorexia; diarrhea; aggravation of peptic ulcer or ulcerative colitis; increased intestinal motility. Cardiovascular—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. Central Nervous System—drowsiness; depression; nervousness; paradoxical anxiety; nightmares; rarely parkinsonian syndrome and other extrapyramidal tract involvement; CNS sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, and optic atrophy). Muscular—muscle aches; myalgia; muscle cramps; dryness of mouth; digitalis toxicity; dizziness; syncope; epistaxis; purpura and other hematological reactions; impotence or decreased libido; dysuria; muscular aches; conjunctival injection; weight gain; breast engorgement; pseudotumor; gynecomastia; early water retention with edema in hypertensive patients.

Hydralazine: Common—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. Less frequent—nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremor; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity; constipation; difficulty in micturition; arthralgia; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura.

Hydrochlorothiazide: See hydrochlorothiazide section above.

DOSEAGE

Esimil
Optimal dosage must be determined for each individual. Note: 10 mg guanethidine monosulfate present in Esimil is equivalent to 8.4 mg guanethidine sulfate USP (Ismelin®).

Before starting therapy, consult complete product literature.

Ser-Ap-Es
One or 2 tablets I.D. To initiate therapy, 1 tablet I.D. is recommended. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.

HOW SUPPLIED

Esimil
Tablets (white, scored), each containing 10 mg guanethidine monosulfate and 25 mg hydrochlorothiazide; bottles of 100.

Ser-Ap-Es
Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 100 and 400.

Consult complete literature of both products before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

24129 17

C I B A

Cytomegalovirus Disease

STOCKHOLM—It is conceivable that an impaired ability of lymphocytes to produce interferon is related to the appearance of congenital cytomegalovirus disease with severe symptoms, said Dr. G. Emodi, of University Children's Hospital, Basel, Switzerland.

About 1 per cent of newborn infants excrete cytomegalovirus in the urine, and most of these have demonstrable viremia for several months, he told the annual meeting of the Swedish Medical Society. Furthermore, one in 30 newborns with cytomegaluria shows clinical symptoms of congenital cytomegalovirus infection.

Dr. Emodi studied four groups: children with congenital cytomegaluria and severe clinical symptoms, children of the same age with and without viremia, mothers of the first group without clinical symptoms but with viremia, and healthy laboratory personnel without cytomegaluria.

He found that the interferon-producing capacity of peripheral lymphocytes in vitro from the congenitally severely ill children was greatly reduced. The other groups were able to produce 60-70 per cent more interferon.

Trachoma Incidence Drops

JOHANNESBURG, SOUTH AFRICA—The incidence of trachoma in South Africa has dropped dramatically in the past 15 years, from 40 per cent to only 6 per cent.

A project in which 60,000 Bantu children in the Northern Transvaal have been treated annually is credited for what is considered one of the greatest success stories in the country's preventive medicine program.

"In addition, the gravity of the disease is so low today that one can confidently predict that no child in the area where we have been working will ever go blind from trachoma," Dr. J. Graham Scott, project head, told delegates to the biennial conference of the South African National Council for the Blind.

A white supervisor and four trained Bantu field workers are now beginning a training program in 40 Northern Transvaal schools to show teachers how to use the antibiotic ointment that has proved so effective.

Down's Syndrome

STOCKHOLM—A deficiency in catecholamine metabolism may exist in Down's syndrome, it was suggested at the annual meeting of the Swedish Medical Society by Dr. Karl-Henrik Gustavson, of University Hospital, Uppsala.

He reported that five-to-15-year-old children with the syndrome showed significantly lower dopamine-β-hydroxylase (DBH) activity in the plasma than normal controls and nonmongoloid mentally retarded children. The last, in turn, had a significantly lower DBH activity than controls.

Dr. Gustavson said he has also found the catechol-O-methyltransferase activity in the erythrocytes of Down's sufferers to be significantly higher than in normal children.

First-Cousin Marriages

TEL AVIV, ISRAEL—About 10 per cent of the number of retarded children in Israel are the issue of first-cousin marriages, according to Dr. Bernard Cohen, of the Sheba Medical Center.

Calling for a ban on such unions, Dr. Cohen said that consanguineous marriages (first cousins and uncle-niece pairs) run as high as 26 per cent of all marriages in some Jewish ethnic communities, such as the Persian. He put the rate at 22.8 per cent among Iraqi, 12 per cent among Yemenite, and 9 per cent among Moroccan Jews.

Among Ashkenazi (European and American) Jews, the rate is only 1.52 per cent, he said.

Stimulants Are Used to Treat Hypersomnia

Medical Tribune World Service

BASEL, SWITZERLAND—The use of amphetamines or similar stimulants to treat hypersomnia and "sleep drunkenness" is advocated by a Prague neurologist, who says patients do not become addicted to the drugs even after a long period.

After such treatment, patients report that they sleep better than before, if not so deeply, and feel that their sleep is more nearly normal, Dr. B. Roth, of Charles University, told the first European Congress for Sleep Research here.

"Sleep drunkenness is a distinct clinical entity," he declared, "and it occurs in approximately one-third of all hypersomnia cases."

Unfortunately, it is unknown to most physicians, Dr. Roth told MEDICAL TRIBUNE in an interview, especially because they never ask the patient the most pertinent question: how does he wake up? They ask, Dr. Roth said, only if the patient has difficulty staying awake during the day and how he sleeps.

He suggested that the physician ask the patient four questions when hypersomnia is suspected:

- How do you fall asleep in the evening—without difficulty? rapidly?

- How is your night's sleep? Do you sleep well? badly?
- How do you wake up?
- How about staying awake during the day? Is it difficult?

How the patient wakes up can be important, Dr. Roth explained, because it may mean he has sleep drunkenness as well as hypersomnia. Such patients have what he terms a hypersomninc state during the day, with several irresistible sleep periods of two hours or so. At night they fall asleep quickly and sleep deeply and long. If left to sleep until spontaneous awakening, they sleep for 15 to 16 hours at a time.

If someone wakes them in the morning, they have symptoms of sleep drunkenness, are disoriented and confused, and will return to bed and go on sleeping if allowed to. It is necessary to awaken them "very aggressively and for a long time," and even then they are unable to work. Their efficiency remains low until evening.

It is in such cases that Dr. Roth advocates the administration of amphetamine at bedtime. The patients then wake up in the morning without difficulty, he said. There are patients who do not tolerate

this treatment, however, because it disturbs their sleep. In these cases, Dr. Roth changes the hour of giving the stimulant. Someone else in the family awakens the patient about half an hour before it is time for him to get up, makes him take the drug, and then lets him go to sleep again. Half an hour later, he will hear the alarm and awaken without his sleep drunkenness.

Some of Dr. Roth's patients have been receiving this treatment for years, with no inconvenience and without necessity to increase the dose, he said.

He believes that most hypersomnics who also suffer sleep drunkenness can be helped enough by amphetamine treatment to hold jobs and live normal lives.

Institute Set for Studies Of South African Disease

Medical Tribune World Service

PRETORIA, SOUTH AFRICA—The Hans Snyckers Institute for the study of diseases endemic to South Africa will be set up at Pretoria University. It is to be created by a grant from a South African pharmaceutical firm and affiliated with the university's medical faculty.

Wednesday, February 21, 1973

Stamps

Joaquim Duarte Murtinho



Joaquim Duarte Murtinho (1848-1911) was born in Culaba, Brazil. He studied medicine at the Medical Faculty of Rio de Janeiro and received his degree in 1872. He was a general practitioner and then a teacher of clinical medicine.

Following the formation of the Brazilian republic in 1889, he was elected senator from his home state of Mato Grosso. Politics became his main interest, and he was named Minister of Industry and Public Works, and later became the Minister of Finance.

Brazil issued the stamp in 1954 to honor Murtinho as a statesman. 1973 marks the 125th anniversary of his birth.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

SLE May Worsen on Azathioprine Withdrawal

Medical Tribune Report

PITTSBURGH—Abrupt withdrawal of azathioprine therapy in systemic lupus erythematosus is frequently followed by exacerbation of the disease, according to investigators from the State University of New York Downstate Medical Center.

Patients should therefore be closely observed for at least six months after such withdrawal, they cautioned.

"The difficulties in discontinuing azathioprine therapy, once initiated, and the unknown risks of long-term azathioprine administration, necessitate careful reconsideration of the indications for use of this potent drug," they told the 18th interim scientific session of the American Rheumatism Association here. The investigators were Drs. Ezra Sharon, Herbert S. Diamond, and David Kaplan.

The 16 women patients in the study had all received azathioprine 2.5 mg./Kg./day for at least 18 months, were in remission, required less than 15 mg./day prednisone or its equivalent, and had creatinine clearance greater than 50 ml./minute and blood urea nitrogen less than 30 mg./100 ml. Nine of the patients were randomly selected for azathioprine withdrawal while maintaining their usual dose of other drugs,

and seven patients were continued on azathioprine. All the patients were followed for one year.

Seven of the nine patients in the withdrawal group and one of the seven in the continuation group experienced an acute exacerbation of their disease, the investigators reported. In the withdrawal group, exacerbations occurred 21 to 200 days after azathioprine therapy was halted; in four of these seven patients this occurred between 80 and 105 days later. In the single patient in the continuation group, it occurred 225 days after entrance into the study.

Five of the patients from whom the drug was withdrawn and the one in whom it was continued required hospitalization, the physicians reported.

In the withdrawal group the exacerbation was manifested in two patients by acute episodes of cerebritis and in four others by multisystem activity, including pleuritis, arthritis, and rash; the seventh patient, who died, had acute relapse of her disease with fulminant nephritis. The patient in the continuation group who suffered exacerbation developed anemia and deterioration of renal function.

Initial treatment of exacerbations in the

withdrawal group was by increasing the dose of prednisone. If control of the disease was not achieved when the corticosteroid dose was doubled or if life-threatening complications developed, azathioprine therapy (2.5 mg./Kg./day) was reinstituted and corticosteroid was further increased.

"At the end of the 12-month study period," the investigators reported, "seven of the nine patients in the withdrawal group had required reinstitution of azathioprine in accord with the above criteria."

Noting that the 78 per cent incidence of exacerbation following abrupt withdrawal of azathioprine is "disturbing" and raises the possibility that abrupt discontinuation may in some manner provoke the exacerbation, the physicians suggested the possibility "that a decreased incidence of relapse might follow gradual tapering of the azathioprine dosage to the point of discontinuance."

Psoriatic Arthritis Described From a Study of 8 Children

From Worcester, Mass.

Noting that reports of psoriatic arthritis in children are "quite scanty," a team of Worcester, Mass., physicians described a study of eight children with this disorder.

Drs. John J. Calabro and Shanker L. Garg, of the University of Massachusetts Medical School and the Worcester City Hospital, remarked that the paucity of reports "is rather surprising, for the peak age of onset of psoriasis is predominantly between five and 15 years."

The eight patients, five girls and three boys, were followed for two to 14 years. Ages at onset ranged from eight to 15 years. In five of the children psoriasis and arthritis began simultaneously, and in three psoriasis developed one to four years after arthritis.

The initial arthritis was monarticular in three of the patients (a knee in two and a wrist in one) and polyarticular in five. All of the latter and one of the former had arthritis of the distal interphalangeal (DIP) joints.

Nails Usually Affected

In all but one of the patients the nails were affected, the effects varying from minimal thickening and ridging to "distinctive pepper-pot pitting, discoloration, and onycholysis." In none of the patients was there rheumatoid factor, antinuclear antibody, or hyperuricemia.

"The subsequent pattern of arthritis of all patients," the report said, "has been intermittent, with long periods of remission and relatively short episodes of active synovitis. Recurrent arthritis was often asymmetric and with frequent DIP involvement; it was oligoarthritis (involving one to three joints) in three patients and polyarthritis in five, two of whom had a clearcut temporal relationship between acute flares of psoriasis and recurrent arthritis."

Currently, the investigators said, no patient has developed arthritis mutilans or spondylitis; all eight patients are in ARA functional classes I and II, and five are in remission.

A comparison of the eight patients with 100 patients with juvenile rheumatoid arthritis revealed the following features: there was a later age of onset—mean age of 12.5 years compared with 6.8 in the JRA group; prominence of DIP arthritis and sausage digits; and paucity of systemic manifestations, including fever, lymphadenopathy, and splenomegaly.

The investigators acknowledged that the number of patients studied was too small for meaningful statistical analysis.

Drug Names in Pakistan

Medical Tribune World Service

KARACHI, PAKISTAN—A bill providing for the adoption of generic names for drugs has passed the National Assembly of Pakistan. The measure also calls for standardization of the manufacture of drugs by a national formulary.

R.S.V.P.



She just doesn't respond to things. No interest. No energy. Discouraged.

It may be mild depression. She needs help...and she needs it now.

Counsel and reassurance may suffice. But if you decide supportive medication is indicated, Ritalin may offer prompt benefit.

Ritalin usually begins to act with the very first dose...boosts spirits and brightens mood...helps the patient get moving again. And Ritalin is generally well tolerated, even by older and convalescent patients. However, Ritalin should not be used for severe depression.

When Ritalin works, one prescription may be enough...to help provide an answer to mild depression.

Ritalin® (methylphenidate) helps the patient respond in mild depression*

Ritalin® hydrochloride (methylphenidate hydrochloride) TABLETS

INDICATION
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indication as follows:
"Possibly" effective: Mild depression
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS
Ritalin is not recommended for children under six years, since safety and efficacy in this age group have not been established. Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative. Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS
Patients with an element of agitation may react adversely; discontinue therapy if necessary. Periodic CBC and platelet counts are advised during prolonged therapy.

ADVERSE REACTIONS
Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, arthritis, exfoliative dermatitis, and erythema multiforme with histopathological findings of necrotizing vasculitis); anorexia; nausea;

dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmias; abdominal pain; weight loss during prolonged therapy. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently. Toxic psychosis has been reported.

DOSEAGE AND ADMINISTRATION
Adults: Administer orally in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Dosage will depend upon indication and individual response.

Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. If medication is taken late in the day should take the last dose before 6 p.m.

HOW SUPPLIED
Tablets, 20 mg (pale green, scored); bottles of 100 and 1000.
Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1000 and Strip Dispensers of 100, 500 and 1000.
Tablets, 5 mg (pale yellow); bottles of 100, 500 and 1000.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

34-0000 22

This drug has been evaluated as possibly effective for this indication. See brief prescribing information.

C I B A

Excessive Anxiety in the Duodenal Ulcer Patient...

The Somatic Protest

The contributory role of anxiety in the pathogenesis and exacerbation of peptic ulcers is well established. Thus, excessive emotional tension and anxiety are believed to cause adverse changes in the physiology of the stomach or duodenum.

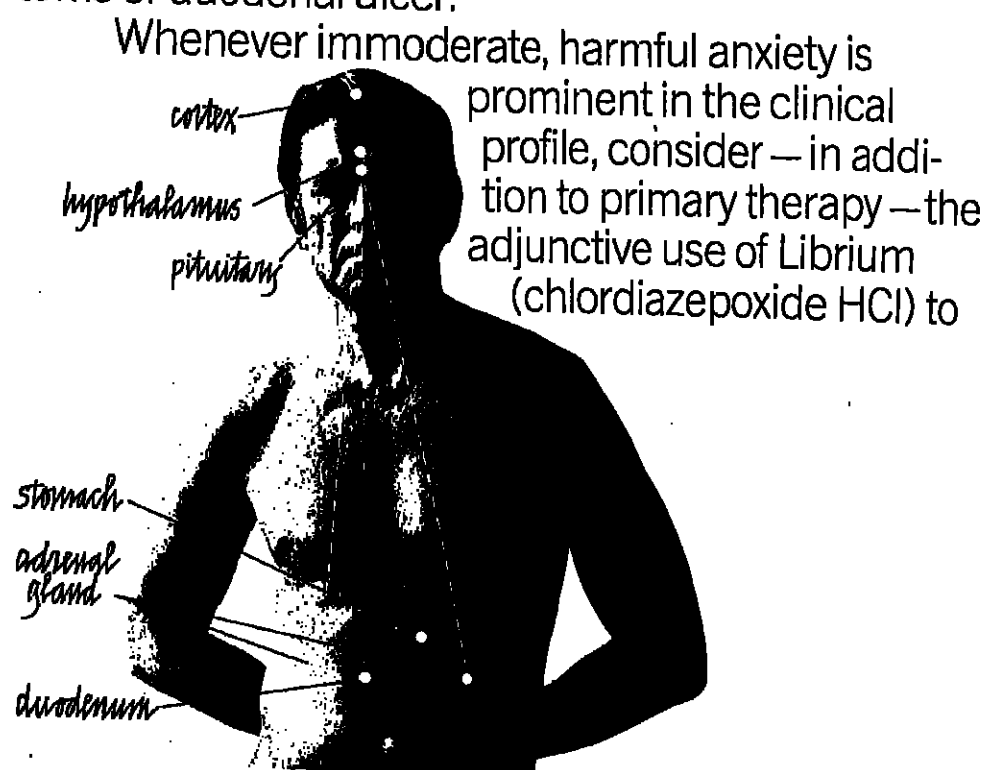


Large ulcer in the midportion of the duodenum well demonstrated on spot films

Although the exact mechanism of these changes remains to be elucidated, it appears probable that the central nervous system as well as its chief neural and humoral outflows are involved. In many patients with duodenal ulcer, gastric hypersecretion and intestinal hypermotility are the end-organ manifestations of these processes and usually give rise to the typical symptoms of duodenal ulcer.



Compression spot films of duodenum



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g.,

operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical

reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG

patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

For moderate
to severe anxiety
adversely affecting
gastrointestinal
function

adjunctive
Librium® 10 mg
(chlordiazepoxide HCl)
1 or 2 capsules t.i.d./q.i.d.

Top Health Programs May Be Budget Victims

Continued from page 1

(HEW has not had an official budget for fiscal 1973. The Administration's first budget was altered by appropriation bills that were then twice vetoed. The department is now financed under a "continuing resolution" arrangement—and the Administration has revised some of its original budget proposals.)

But the lion's share of the 1974 projected increase—about \$3 billion of the \$3.88 billion—consists of the expected rise in outlays for Medicare and Medicaid benefits. And of the remaining \$828,000,000, the lion's share will be backstop budget orphans. Thus, \$636,000,000 is requested as the budget authority needed between now and 1980 to honor Federal staffing grant commitments already made to community mental health centers. About \$100,000,000 is requested to support the neighborhood health centers that are to be transferred to HEW from the slated-for-extinction Office of Economic Opportunity.

Hill-Burton Program

Termination of the Hill-Burton program would end Federal spending for building or renovating hospitals and clinics. Inaugurated 26 years ago, this legislation has channeled some \$3.8 billion towards the construction or modernization of facilities containing more than 480,000 hospital beds throughout the country.

The decision to wind down the program with the 1973 fiscal year is justified for several reasons, according to the HEW budget report. The supply of hospital beds now "appears to be adequate on a national basis." Systems of cost accounting and reimbursement for medical care now permit the depreciation of physical plants to be covered in hospital charges. And finally, the "private capital market" for construction loans is expanding.

RMP Termination

The proposed termination of the Regional Medical Programs would abolish an educational and service network established seven years ago. Financed by about \$500,000,000 over that period, the programs have been the joint effort of more than 50 nonprofit organizations, ranging from medical societies and voluntary health agencies to medical schools.

Goals have included the more rapid dissemination of new scientific information, continuing education for physicians and other health professionals, training in new technologies, development of innovations in health care delivery, and regionalization of complex diagnostic and treatment methods.

The revised Administration budget for fiscal 1973 requests \$60,000,000 for this program, with support to end next June. The HEW budget report says the program "has yet to define a consistent role for itself" and that nearly all of the RMP projects overlap other project grant programs.

Training Grants

Research training grants and fellowships of the National Institutes of Health will be terminated as soon as previously approved grants run out.

Such grants—which are awarded to persons at medical schools and teaching hospital centers—cost \$186,000,000 in 1972, out of a total NIH budget for biomedical research of \$1.47 billion. The revised 1973 budget cut this allocation for research training to \$150,000,000, and the 1974 budget brings the amount down to \$129,000,000. Approximately half of the funds support trainees, while the other half is used to support faculty.

Also to be terminated are the training grants and fellowships in general mental health awarded through the Health Services and Mental Health Administration. The 1974 allotment of \$72,376,000 represents a cut of nearly \$42,000,000 from the 1972 budget, and will be used only for commitments already made.

Three reasons are cited for the decision to terminate support for the training of scientific personnel: the need for a greater number of trained biomedical research scientists "has passed"; it is now possible to rely on "the normal mechanisms in the professional manpower market" to produce any additional investigators; and the "income expectations" of such scientists are sufficiently high that they should pay for their training themselves.

NIH Biomedical Research

The total amount of Federal funds proposed for NIH biomedical research is \$1,532 billion, which is about \$49,000,000 more than the revised Administration budget for 1973 requests. It is some \$37,000,000 less, however, than the amount that had been requested in the original Administration budget for 1973.

Two institutions will receive more funds under the 1974 budget. The National Cancer Institute allotment will rise to \$500,000,000, from \$426,000,000 in the revised 1973 budget. The National Heart and Lung Institute allotment will be increased to \$265,000,000, up from the \$247,000,000 called for in the revised 1973 budget.

All of the other research institutions will have their funds reduced—a total cut of \$43,000,000.

Mental Health Centers

The ending of Federal support for the Community Mental Health Centers program would mean that the 515 centers set up through the Health Services and Mental Health Administration during the past nine years will be expected to rely for financing on individuals, state and local governments, and reimbursements from third-party payment systems.

These centers provide treatment near the home for persons with emotional illness, reducing the need for more expensive long-term and custodial care in institutions. The HEW budget report says that the "workability" of the concept has been "thoroughly demonstrated" but comments that the current momentum "should be adequate to maintain existing centers and stimulate the establishment of new centers."

A sum of \$636,000,000 is requested in the 1974 budget to cover all previously approved commitments for the community mental health centers until the last grant runs out in 1980.

The termination of Federal support for

the CMHC program will also end support for project grants made to such centers for combating alcoholism and drug abuse. Formula grants to state governments for alcoholism programs will continue (\$30,000,000 in 1974). Formula grants for drug abuse programs will amount to \$15,000,000, and project grants will be made under the auspices of the Special Action Office on Drug Abuse Prevention.

Health Manpower Funds

Funds for the training of "health manpower"—physicians, dentists, veterinarians, optometrists, podiatrists, pharmacists, public health specialists, nurses, and allied health personnel, such as technicians—would be cut in 1974 to \$386,000,000. This is a drop of \$38,000,000 from the revised 1973 budget and one of \$292,000,000 from the 1972 budget.

Specific items to be terminated in the 1974 budget include:

- Capitation payments to institutions other than schools of medicine, osteopathy, and dentistry.
- Scholarships, except those for students "who commit themselves to serve in a Federal health program to meet a national need." Scholarships already in effect will be honored. The new National Health Service Scholarship Program will be supported for \$23,000,000.
- Institutional support to schools of public health and allied health, and all assistance programs for students in such schools.
- All construction grants for schools that prepare health manpower.

Direct loans to students of medicine, osteopathy, dentistry, and nursing will be provided at the same level or slightly above that provided in 1972. Amounts set aside for scholarships will decrease, in line with the ban on any new scholarships except for students agreeing to work after their training is complete for a period of time in such Federal programs as the Indian Health Service or the National Health Service Corps.

Medicare, Medicaid

In areas of health spending that would directly affect medical practice, the new budget proposals would produce a tightening of regulations about treatment to be paid for under Medicare and Medicaid.

Under legislation previously passed, states will suffer a loss of matching Federal funds unless they establish an effective utilization review system for Medi-

Fetus, Neonate Research



In researching medical complications of the fetus and neonate, Dr. Peter Hahn determines the activities of the citrate cleavage enzyme in fetal tissue in his laboratory at the new Center for Developmental Medicine at the University of British Columbia in Vancouver.

coid patients. Both preadmission review and predetermination of length of stay are required.

The 1974 budget includes an increase in funds that will be spent to check on services paid for under Medicaid and Medicare. A nationwide network of Professional Standards Review Organizations is being established (financed by \$34,000,000) "through which practicing physicians will assume responsibility for reviewing, on a comprehensive and integrated basis, the necessity for, and quality of, institutional and outpatient services under Medicare and Medicaid."

Medicare patients, in turn, will be required by the proposed budget to increase the proportion of health costs that they pay for out of their own pockets. If they are hospitalized or treated in an extended-care facility, they will pay the first day's actual room and board charges and then pay daily amounts equal to 10 per cent of actual charges.

The Medicare patient's responsibility for medical bills would also increase. The present deductible of \$60 would go up to \$85, and patients would pay 25 per cent rather than 20 per cent of subsequent medical bills.

Fetal Skin, Blood Sampled in Amniocentesis

Continued from page 1

Mammalian Cytology Society to report his cumulative results after 230 diagnostic amniocenteses, but it became clear that cytogeneticists were more eager to hear about tissue cells than about free-floating units.

Dr. Valenti uses an adaptation of a pediatric cystoscope for looking through the uterine wall. With the instrument, he said, he can see exactly what he is doing to the fetus.

"My slides don't show half what I can see at the table," he said. "I can actually count the dermatoglyphic ridges on the fetal hand through my scope."

Before he makes his small incision, usually 2 inches below the pubic hair line, the Professor of Obstetrics and Gynecology at the State University of New York College of Medicine, Brooklyn, uses ultrasound to check location of the placenta. If it is partially anterior, he goes in a little higher, but if the structure is entirely anterior, he does not operate.

Dr. Valenti has now looked at a score of fetuses, moved his scope along the cord proximal to the placenta, sampled cord blood, and moved it back toward the fetus and nipped off a tiny sample of epithelium at the shoulder.

"There is no bleeding from this superficial wound, which does not penetrate the dermis," he said. "That's probably because the amniotic pressure precludes

hemorrhage from the small vessel. I can't imagine there being a visible scar with cell replication proceeding at such a rate, but obviously that's a factor I haven't been able to check as yet."

All of Dr. Valenti's subjects now stay on in the hospital for their abortions, of course, but he plans to keep his early diagnostic mothers for three days while they undergo continuous and intensive monitoring for fluid leakage, fetal heart response, evidence of uterine contractions, and so forth. If the early cases turn out well, he visualizes a 10-10 A.M. procedure, with the mother out and home by the following afternoon.

And here is where the tissue specimen contributes a bonus in time as well as knowledge, he continued. "Not only do we know what we're culturing, but we get new growth in 72 hours, where it now takes 11-12 days for those free-floating cells to stabilize and replicate." This means, he added, that even for metabolic defects, skin biopsies could produce a fetal diagnosis in a week.

The availability of blood for examination, he declared, would mean that much of the controversy over sickle cell anemia might be obviated because the fetus with the most severe sickling could be detected in utero.

Dr. Valenti acknowledged that there is no uterine therapy at present, but he said: "At the time such treatment becomes available, we have to be ready to apply it. And we'll be able to do that by inserting the needle through this instrument."

He compares uterine therapy with early cardiac catheterization of the week-old baby: "They lost some patients in the first few procedures, but now it's become routine."



DR. VALENTI

Mexico Needs Physicians

Medical Tribune Report

NEW YORK—An "urgent" appeal has been issued for physicians and surgeons to work on overseas teams maintained by MEDICO, a service of CARE.

Needed immediately, the organization said, is a general practitioner or pediatrician, interested in public health and knowledgeable in tropical medicine to serve at a new MEDICO installation in Nueva Guinea, Nicaragua. The physician will direct a program of preventive medicine and health education. Information may be obtained from Leonard Coppel, director of contract personnel, MEDICO, 660 First Avenue, New York, N.Y., 10016.

Wednesday, February 21, 1973

Physician-Inventor Devises Hydraulic Football Helmet

Medical Tribune Report

GAINESVILLE, FLA.—Dr. J. Robert Cade, the inventive physician who originated the medicinal thirst quencher Gatorade, particularly for athletes, has now developed a hydraulic helmet designed to protect the wearer against virtually all head injuries.

The helmet—officially known as the Hydra-Flo helmet and colloquially called a "water helmet"—is lined with small vinyl bags filled with water and glycol.

Dr. Cade, Professor of Medicine at the University of Florida College of Medicine and chief of renal medicine at the J. Hillis Miller Health Center here, said the helmet already is being used by some football players on nearly all pro teams and on many college and high school teams all over the country.

The water helmets have been marketed commercially since last spring, and the physician-inventor estimates that about 10,000 of them are now in use. A "youth model" for boys in the eight-to-15 age group was introduced recently.

"No one is sure of the number of head injuries in football games," Dr. Cade told MEDICAL TRIBUNE. "In every game several players have concussions. The players may not be knocked out but they are often confused for a few seconds. In all probability they have had small hemorrhages. I believe this helmet can prevent these brain concussions."

Dr. Cade said that the Hydra-Flo helmet has been tested in the Wayne State University Laboratories in Detroit, where all helmets manufactured in this country are tested, and that it has proved to be the most effective in preventing head injuries.

The doctor tried out his invention himself by putting it on and getting a colleague to hit him over the head with a two-by-four.

"It made a lot of noise," he said, "but it didn't hurt me."

Dr. Cade said the helmet would provide protection from head injuries for motorcycle riders as well as football players.

Has Lighter Shell

The Hydra-Flo device is made of plastic with a slightly lighter shell than a conventional helmet. It is lined with a layer of plastic foam and 13 interconnected vinyl compartments, containing 16 ounces of water and propylene glycol, guaranteed not to freeze at temperatures as low as -45° F. The principle behind the water helmet is that the fluid inside the bags will protect the head by absorbing and diffusing the shock of impact.

"The water absorbs and diffuses energy before it gets to the head and brain," Dr. Cade explained.

The equipment's only drawback, he said, is the possibility of an occasional leak in one of the bags.

"A little fluid may squirt out," he said, "but even so, the helmet continues to work effectively."

Dr. Cade began to develop a better football helmet about seven years ago.

"George Dean, a defensive end for the Florida football team in 1965, had a couple of concussions that were relatively serious," he recalled, "and that's when I began thinking about making a better helmet."

Dr. Cade produced his first helmet by hand with the help of a tire and rubber company in Gainesville. The water helmets now in use—the third modification—are being manufactured by Gladiator Athletic Inc., of Leesburg, Fla.

The headgear costs \$26—compared with about \$23.50 for a conventional helmet. Dr. Cade has received enthusiastic testi-



DR. CADE

monials from a number of football players. For instance, linebacker Willie Lanier of the Kansas City Chiefs has said he "wouldn't wear any other kind during a game."

Football teams all over the country are now using Dr. Cade's other major invention, Gatorade, which was first formulated in 1965 to quench the thirst of athletes and to replenish lost body chemicals.

Dr. Cade said that about 30 imitations of Gatorade have been introduced on the market, but all except two are "dead" now. He added: "They say when you are first with something, you continue to be the leader."

There have been a number of flavoring improvements in Gatorade, and the product is being sold overseas as well as in this country. It is being marketed as a beverage for "active people."

A long legal wrangle over the royalties from Gatorade was ended recently, and Dr. Cade expects sales of the product to increase as a result. Stokely-Van Camp, Inc., which bought the right to market Gatorade, pays a royalty of \$25,000 annually plus 3 cents on each gallon. Dr. Cade and other members of a "Gatorade Trust" will receive 80 per cent of the royalties and the University of Florida will receive 20 per cent.

Drives 1951 Automobile

Dr. Cade insists that the profits from Gatorade have not affected his life-style. He still drives a 1951 Studebaker, affectionately called "Ol' Spot," which has traveled 235,000 miles.

When asked how he's spending his royalties, he replied: "I've put a number of students through medical school and law school. I am trying to raise my own crop of lawyers. I wouldn't be a bit surprised if I should need them!"

Several years ago he developed a high-protein, high-carbohydrate food supplement for athletes, Gator-Go, but it became "too expensive" because of Federal Government regulations.

He explained: "The Government said we had to pay the grade-A price for milk—about 20¢ a pound—when we could get dry milk for only 6 cents a pound."

Dr. Cade is now working on a high-protein orange juice for people who don't like to eat breakfast.

"I began working on it for my sister—who doesn't like to eat breakfast," he said. "The product is made with whole orange juice. It could be sold as a dry powder or as a frozen beverage. One 8-ounce glass of the product would provide one-third of the daily requirement of protein."

As a Professor of Medicine, Dr. Cade has a full schedule and little time for

MEDICAL MEETING SCHEDULE

Foreign Meetings

- March 11-21 ... German Medical Association Postgraduate Congress on Human Genetics and Paediatric Medicine, Davos, Switzerland
- March 12-24 ... German Medical Association Postgraduate Congress on Human Genetics and Paediatric Medicine, Badgastein, Austria
- March 25-29 ... International Symposium on Hepatology, Tel Aviv
- March 27-31 ... Ceylon Medical Association, Anniversary Meeting, Colombo
- April 5-11 ... European Association of Radiology International Diagnostic Course, Davos, Switzerland
- April 9-12 ... International Symposium on Cancer Detection and Prevention, Bologna, Italy
- April 11-13 ... British Society for Cell Biology Annual Meeting, Manchester, England
- April 11-27 ... Massachusetts Medical Society, Midwestern Society District Committee on Postgraduate Medical Education Tour and Seminar, Greece and Italy

Adapted Ergometer Gauges Musculature



The standard bicycle ergometer has been adapted to provide for the measurement of upper body musculature. Frank Pyke, Ph.D., shown above with James Baker, seated, inventor of the device, is using the adapted ergometer in his studies of the metabolic and circulatory responses of canoeists and kayakers at Dalhousie Univ.

writing about or working on his inventions during the day. "I think up most of them," he said, "while driving between my home and office."

Dr. Cade conceded that he's "probably

regarded as a nut" by some but added: "I don't really care what other people think if I think I'm right. I don't mind being the only person in the world who thinks what I think. When I'm the only one, I'm right about half the time!"



"The Physician's Life Cycle," a contribution from Dr. Phillip L. Rossman of Los Angeles, appeared here in November. Dr. George Thomson, of the Medical College of Wisconsin, writes, "I am certain Phillip Rossman produced his 'life-wise' vignettes of the eccentric doctor to stimulate the conscience of your physician readers. Just in case the subtle verbiage escapes anyone, I suggest the following translation from the language of the doctor to that of the physician."

The Rossman version

- I'm going into pre med this year.
- Which is the best medical school?
- Should I take a straight or rotating internship?
- You should see this girl I met!
- Do you think the Army or Navy is best?
- I'm going back for a residency.
- Oh yes, I'm specializing.
- Have a cigar, it was a boy!
- Just passed my boards.
- Should I go solo or group?
- How much a foot for rent?
- Where can I find a good nurse?
- Let me tell you about this case I had.
- What do you get for a gallbladder?
- When do I become a full partner?
- What's good in the stock market?
- How can I get some write-offs?
- Look at this picture of my granddaughter.
- Know where I can get a good assistant?
- You can charge me now, Doc; I'm on Medicare.

The Thomson version

- I'm taking Sociology, Anthropology and Philosophy next year.
- With this background, who will take me into med school?
- Where can I learn the most about patients' problems?
- You would love this girl I met.
- Which service needs me most?
- I've got to learn more.
- Because I'm me, how can I do the most good?
- We had a baby!
- Passed my boards. My peers are impressed, but are my patients?
- How can I best care for our baby and the patients?
- Is there a parking place for the patients?
- Where can I find someone to help me care for patients?
- Let me tell you about this patient I had.
- After the insurance, how much does the patient pay for a gallbladder?
- As a full partner, am I on the utilization review committee?
- Where can I invest to make our community grow?
- The Boy Scouts, our Church and Schmitzkopf's disease are deductible contributions.
- Look at this picture of our granddaughter.
- Know where I can get an associate?
- Thank you for caring for me as a fellow physician.